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EMBRYOLOGY

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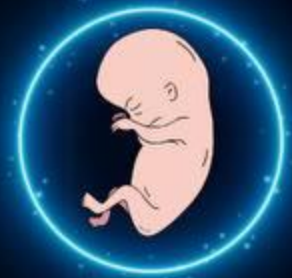

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Respiratory System Embryology

Color code

- Slides
- Doctor
- Additional info
- Important

❑ The flow of information in this lecture:

1. The development of nose and palate
2. The development of Respiratory System .
3. Anomalies (malformation) of trachea and esophagus.
4. The development of the larynx.
5. Anomalies of the larynx.
6. The development of Lungs and Bronchial tree.
7. Anomalies of the lung.

▫ عدد السلايدات كبير شوي

بس لا تقلقوا المحاضرة ان شاء الله سهلة

Say بسم الله and let's start

In the beginning, let's revise some information in embryology:

Germinal Layers:

Ectoderm: Gives rise to the outermost layer of the skin (epidermis).

Mesoderm: Gives rise to various structures, such as bones, cartilage, muscles, blood vessels, and the lymphatic system.

Endoderm: Gives rise to the lining of internal organs, such as the gastrointestinal (GI) tract, respiratory system.

1. Development of the nose and Palate

The development of the nose begins with a structure called the Placode, it is a local thickening in the embryonic ectoderm layer that develops into a sensory organ or ganglion.
The word “Placode” means “the beginning of organ development”, so:
Otic Placode: Involved in the development of the ear.

Lens Placode: Involved in the development of the eye.

Nasal Placode: Involved in the development of the Nose.

Here, imagine the anatomy of the nose (this will help you in understanding the embryo of it), it consists of two anterior openings (nares) and two posterior openings (choana), it consists of two cavities and a septum in between
So how the nose develops?
In the beginning we have **nasal placode**, which is at the beginning of the nasal opening, during 5th week of pregnancy, it will invaginate creating **nasal pits (nostrils)**, (what is the difference between nasal pits and nostrils? According to Chat GPT, the pits is the embryonic origin of the nostrils), these pits are derived from the skin (because the placode is derived from skin (ectoderm layer) ☺). After that, it will invaginate to create the **vestibule** (dehleez), a dilation in the front part of the nose, it is lined with stratified squamous keratinized epithelium, it also contain thick & thin hair that help trap dust.

Another term in embryology is the term “prominence”, when the cells receive a signal it will start to duplicate, creating the prominence (from the nasal placodes), so it means “development of area and proliferation of cells”. This prominence has a goal, like the **frontonasal prominence**, which will participate in the formation of the **nasal septum.**
As the name of the Frontonasal prominence suggest it is a bony prominence originating from the frontal bone and reaches down to the nose forming the nasal septum.
And by mentioning the term “stomodeum”, it refers to a shallow depression on the surface of the embryo that eventually develops into the anterior part of the oral cavity

Also, there’re nasal prominences, there’re medial nasal prominences and lateral nasal prominences, both will contribute in the formation of the nose.
Medial nasal prominences, from the name, it grows to the midline and will contribute in making the septum along with frontonasal prominence (this information had been repeated several times during the lecture).
Lateral nasal prominences will make the lateral wall of the nose.

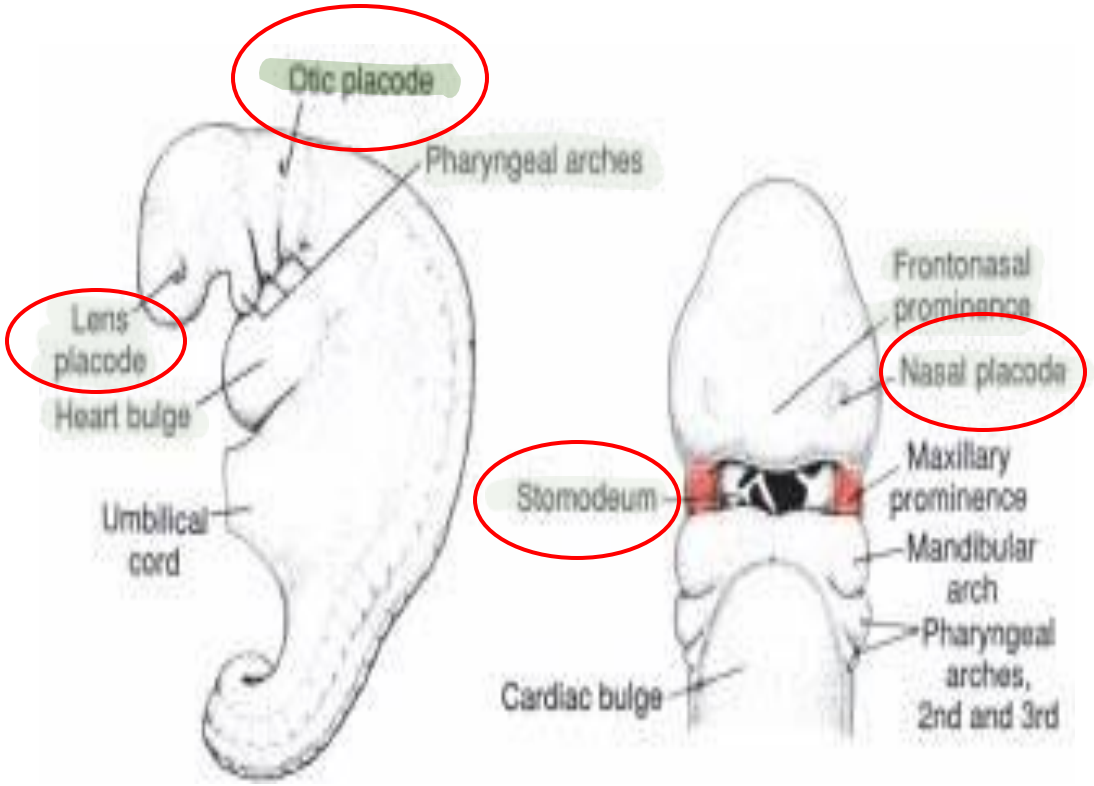
Another prominences:
- Maxillary Prominence: Involved in the development of maxilla, upper lip and the nose.
- Mandibular Prominence: Involved in the development of lower jaw (mandible)

Development of the nose

- At the end of the fourth week (the development always start at the end of the 4th week), **facial prominences** consisting primarily of neural crest-derived mesenchyme and formed mainly by the first pair of pharyngeal arches appear

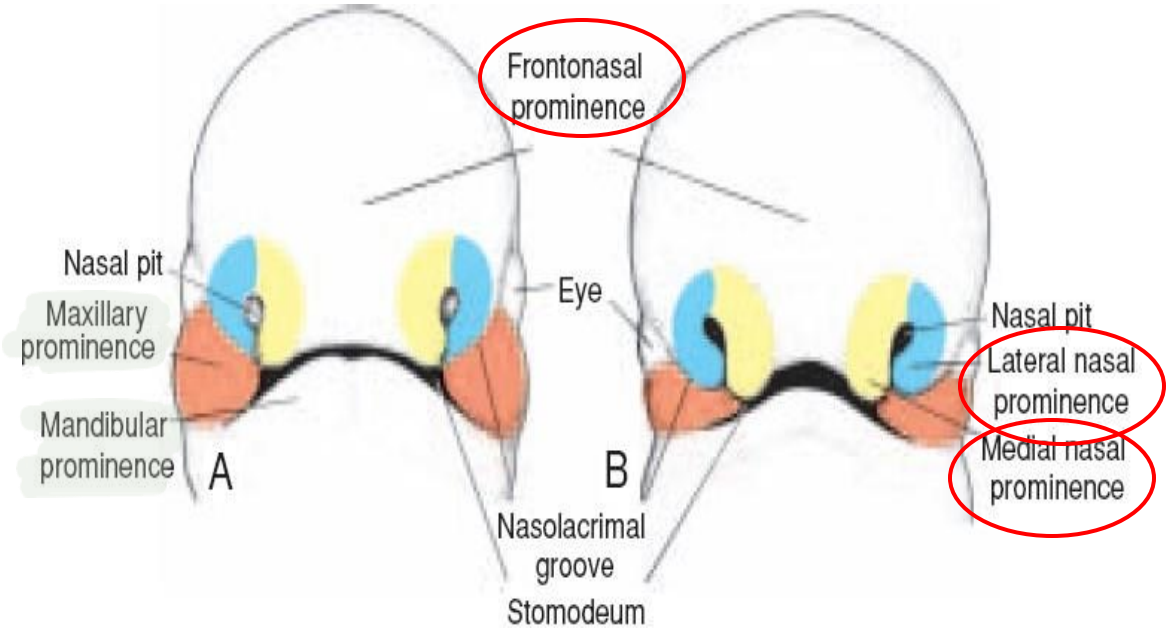
- The **frontonasal prominence,** formed by proliferation of mesenchyme ventral to the brain vesicles, constitutes the upper border of the stomodeum

- On both sides of the frontonasal prominence, local thickenings of the surface ectoderm, the **nasal (olfactory) placodes,** originate under inductive influence of the ventral portion of the forebrain



Development of the nose

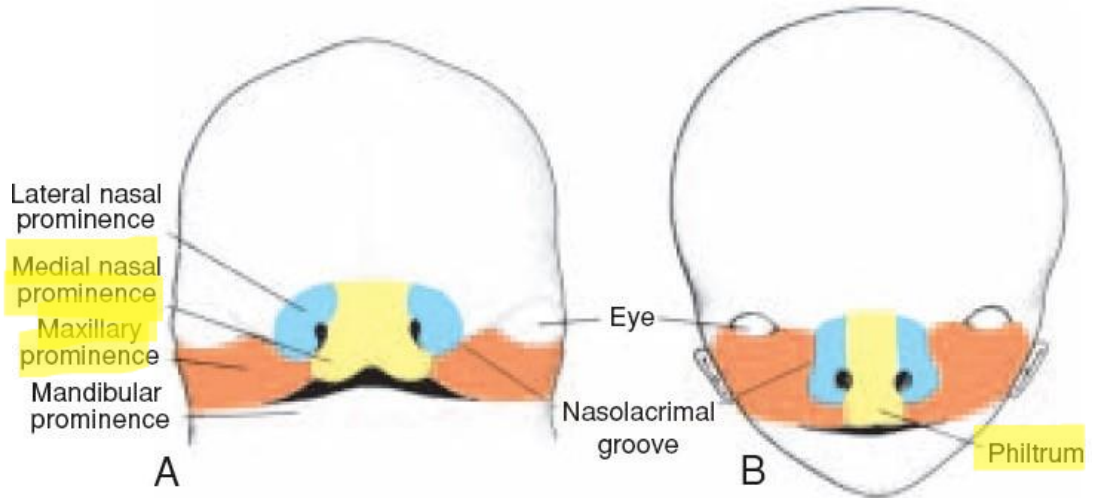
- During the fifth week, the nasal placodes invaginate to form **nasal pits (nostril)** (anterior openings)
- In so doing, they create a ridge of tissue that surrounds each pit and forms the **nasal prominences.**
- The prominences on the outer edge of the pits are the **lateral nasal prominences;** those on the inner edge are the **medial nasal prominences**

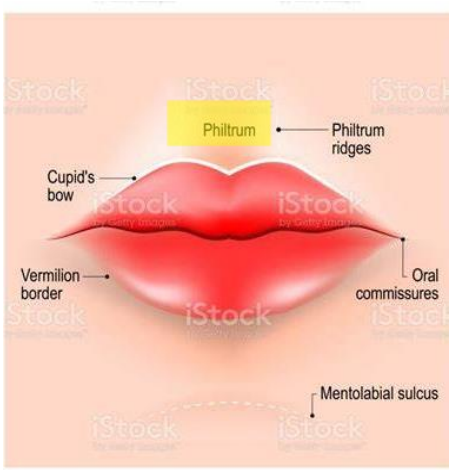


Backing to the medial and lateral nasal prominences, (this is after 2 weeks from the 5th week).

Notice the medial nasal prominences (yellow) in the picture (see how they merged with each other), it covers the midline and all the surrounding, including the **philtrum,** which is a vertical depression on the upper lip. It is formed by the **medial nasal prominence** and meets with frontonasal prominence.

Look again in the picture and notice how the **maxillary prominences** grow to the midline, meet with the **medial nasal prominence and fuse with it**. If this fusion fails, a developmental anomaly known as **Cleft Lip** (unilateral or bilateral) arises.

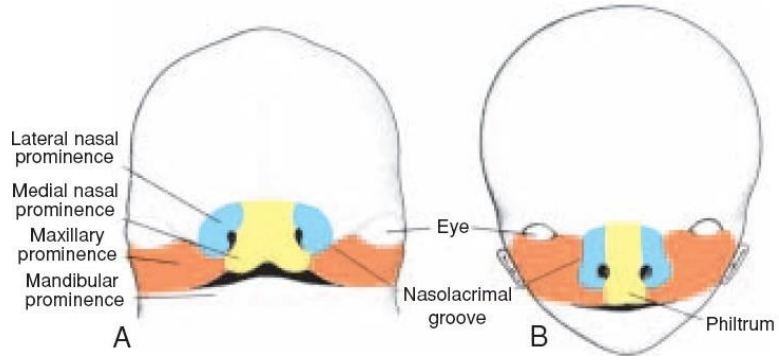




Cleft Lip

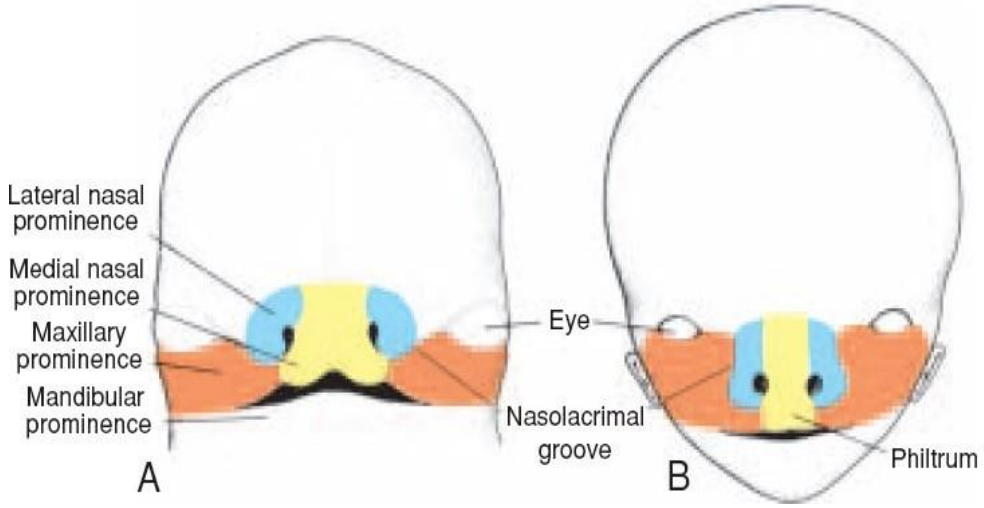
Development of the nose

- During the following 2 weeks, the maxillary prominences continue to increase in size
- Simultaneously, they grow medially, compressing the medial nasal prominences toward the midline
- Subsequently the cleft between the medial nasal prominence and the maxillary prominence is lost, and the two fuse



Development of the nose

- The **nose** is formed from five facial prominences
- the frontal (frontonasal) prominence gives rise to the bridge; and **nasal septum**
- the merged medial nasal prominences provide the crest and tip of the nose;
- the lateral nasal prominences form the sides (alae) and lateral wall of nose
- Olfactory pit forms the nostril (originate from placode) and then becomes deeper (invagination of placode) to form a blind sac (the vestibule)



Development of the nose

- Doctor read all the table

TABLE 15.2 Structures Contributing to Formation of the Face

Prominence	Structures Formed
Frontonasal[a]	Forehead, bridge of nose, medial and lateral nasal prominences
Maxillary	Cheeks, lateral portion of upper lip
Medial nasal	Philtrum of upper lip, crest and tip of nose
Lateral nasal	Alae of nose and lateral wall
Mandibular	Lower lip and lower mandible

[a] The frontonasal prominence is a single unpaired structure; the other prominences are paired.

Summary (from 021)

The nose is formed from five facial prominences.

1. Frontonasal Prominence : Gives rise to the Nasal Septum - Forehead - Bridge of the nose - Medial Nasal Prominence - Lateral Nasal Prominence

2&3. Right & left Medial Nasal Prominences : Give rise to the tip of the nose - Nasal Crest- philtrum - Medial portion of the upper lip

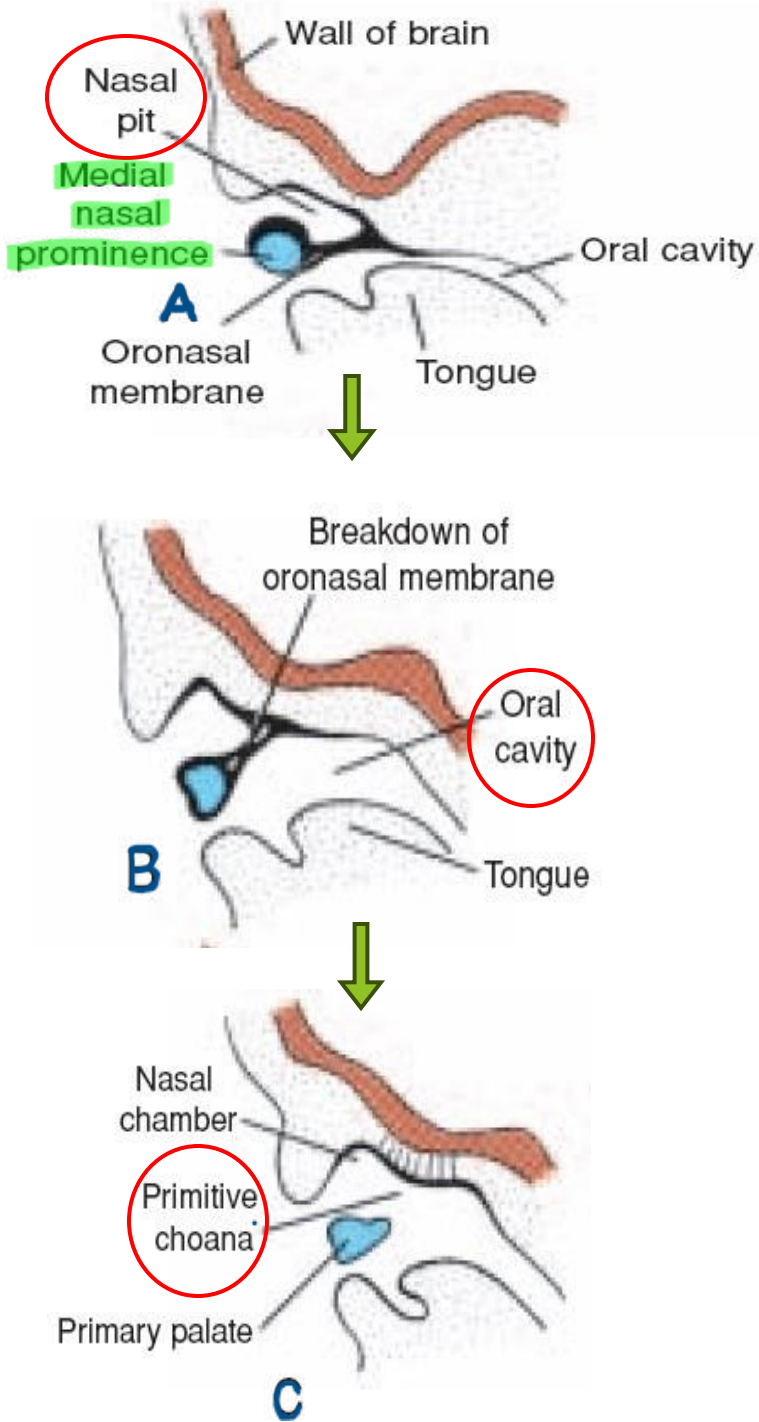
4&5. Right & left Lateral Nasal Prominences: Give rise to the Alae of the nose (lateral wall)

- Maxillary Prominence: Grows internally and is involved in the development of the upper jaw, and the nose.

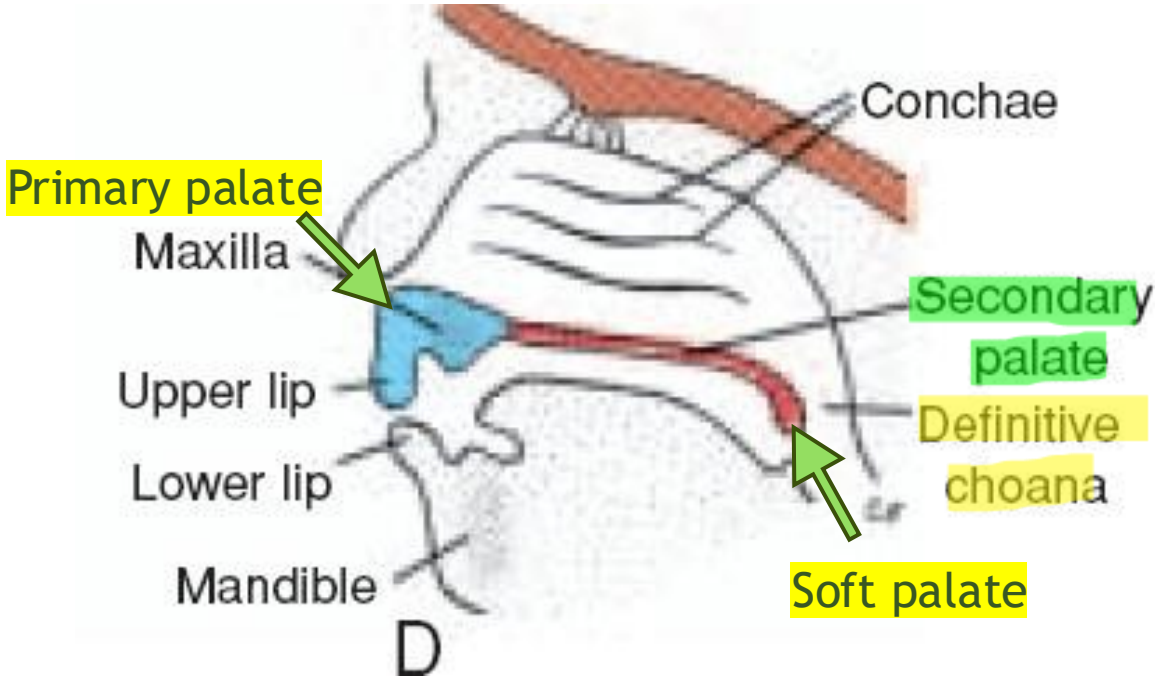
- Mandibular Prominence: Involved in the development of lower jaw and the nose

All the nasal prominences start to proliferate and invaginate (invagination through the mesenchyme) in order to create the nasal cavity, and as clearly stated:
The lateral wall will be developed by lateral nasal prominence
The septum will be developed by frontonasal and medial nasal prominences (Note the medial nasal prominence on the picture)

Look at picture A, notice the Nasal pit that will invaginate in the mesenchyme and create a cavity, the membrane beneath it (which separate the nasal cavity from oral cavity, and will create the hard palate) will rupture and make primary and secondary palate.
The primitive choana started to develop when the primary palate (or membrane) forms and separates the nasal cavity from the oral cavity as in picture C, (while according to the slides and external source, the primitive choana develops when the oronasal membrane disseminate, and it will separate the oral from the nasal cavity, not the membrane or palate in the beginning)
(Note the oral cavity in picture B).

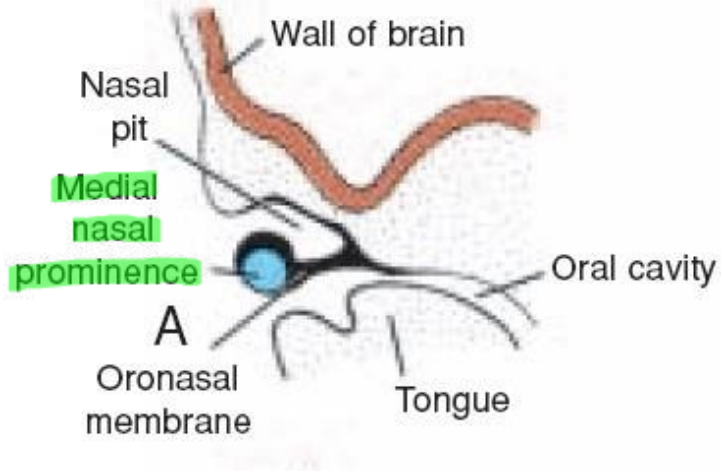


The definitive choana developed, which connects the nasal cavity to the nasopharynx., it developed after the formation of the whole palate
As we said, here the nasal cavity is separated from the oral cavity.
Notice the primary palate, secondary palate and soft palate in this picture



Nasal Cavities

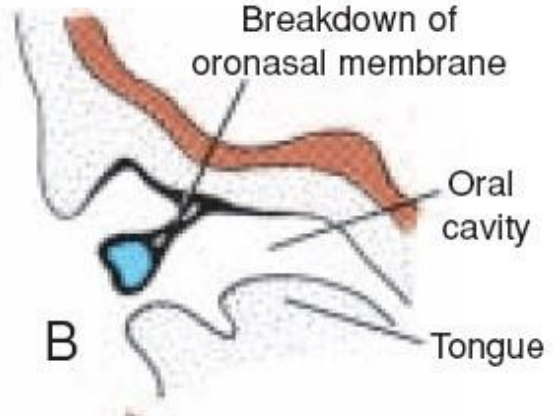
- 1. During the sixth week, the nasal pits deepen considerably, partly because of growth of the surrounding nasal prominences and partly because of their penetration(invaginate) into the underlying mesenchyme

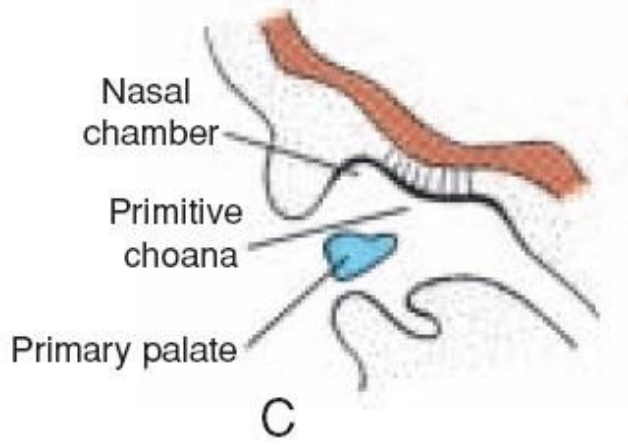


Nasal Cavities

- 2. At first the **oronasal membrane (floor of the nose)** separates the pits from the primitive oral cavity by way of the newly formed foramina, the **primitive choanae**

- These choanae lie on each side of the midline and immediately behind the primary palate.

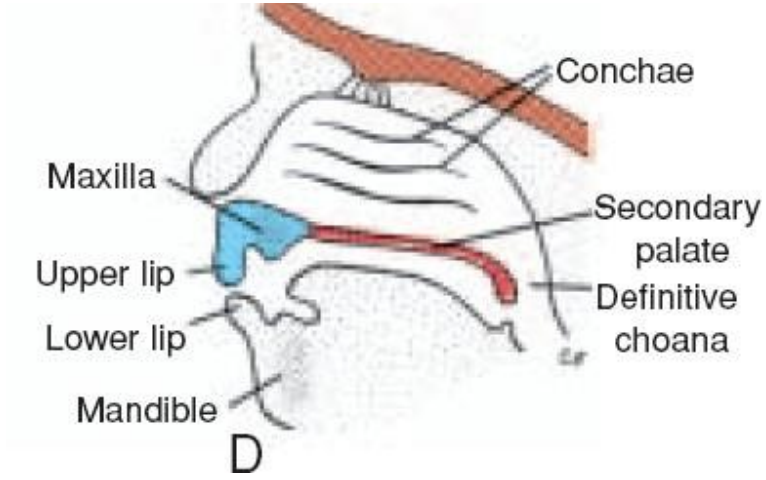




Nasal Cavities

- 3. Later, with formation of the secondary palate and further development of the primitive nasal chambers

- the **definitive choanae will** lie at the junction of the nasal cavity and the pharynx (nasopharynx).



Paranasal air sinuses

- **Paranasal air sinuses** develop as diverticula of the lateral nasal wall and extend into the maxilla, ethmoid, frontal, and sphenoid bones.

- They reach their maximum size during puberty and contribute to the definitive shape of the face.

Every paranasal sinus has a drainage and opening in the lateral wall of the nose.

The development begins from the opening that is in the lateral wall of the nose, it will invaginate until it reaches the bone. For example, if it invaginate backwards and upwards and reach the frontal bone it will make the frontal air sinus, which is a small cavity with an opening and a duct

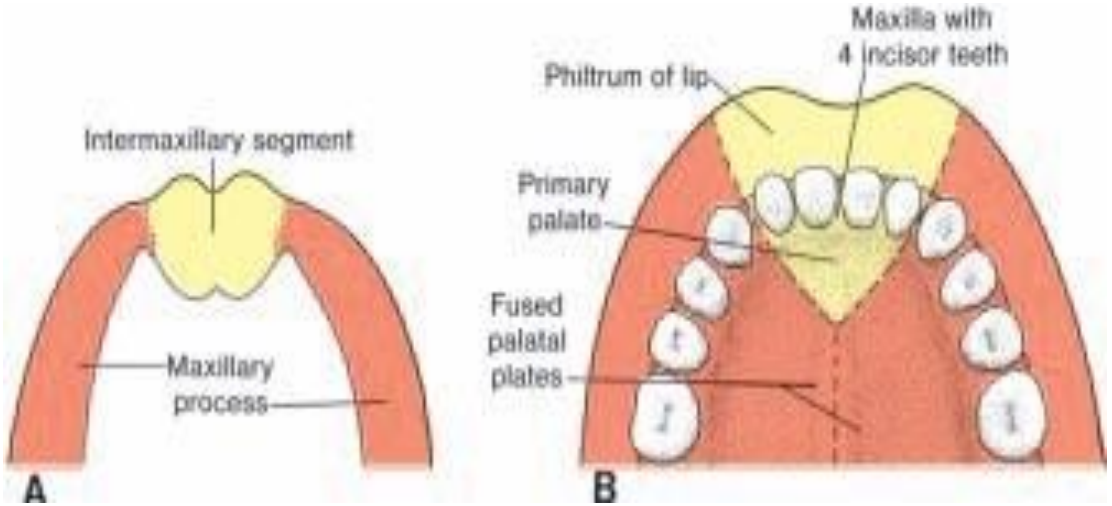
They reach their adult (large) size with the development of the facial bones.

Here we are going to talk about development of Palate

- **I. The development of primary palate:**

The **maxillary prominences** move toward the midline and make **intermaxillary segment alongwith medial nasal prominence (mostly formed by medial nasal prominence),** this segment develop the philtrum in the upper lip, four incisors of the upper jaw and the primary palate which is triangular in shape

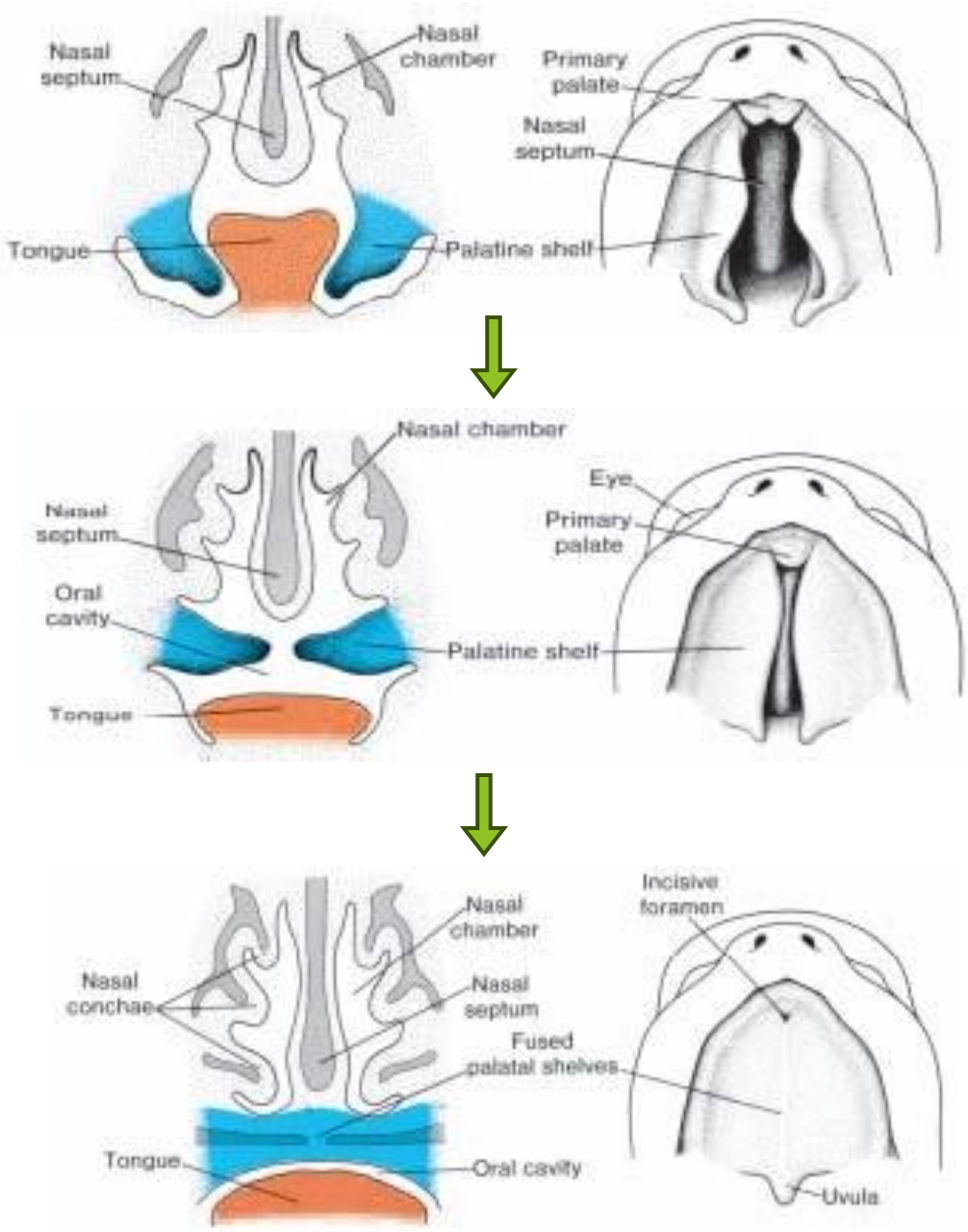
Don't forget that frontonasal prominence (which contribute in the septum) grows forward and downward and meet with this **segment,** in order to separate the 2 cavities of the nose



- **II. The development of secondary palate:** Starts in the 6th week with the development of **Palatine shelves,** which are located at the lateral side of the maxilla, they're directed obliquely downward above the tongue (while the 1st pic shows the shelves on sides of tongue not above it ☺).
- In the 7th week the palatine shelves grow downward to the midline and fuse with each other to form the secondary palate, they will also meet with the primary palate to form the hard palate.
- The 2 shelves fuse with the nasal septum, which will contribute to the 2 nasal cavities.

- **The final resulting structure is the hard palate** (which is primary + secondary palate).

- There's a landmark between primary and secondary palates which is the **incisive foramen**, and there are artery and nerve move through it to reach the nose



Primary palate

- As a result of medial growth of the maxillary prominences, the two medial nasal prominences merge not only at the surface but also at a deeper level.

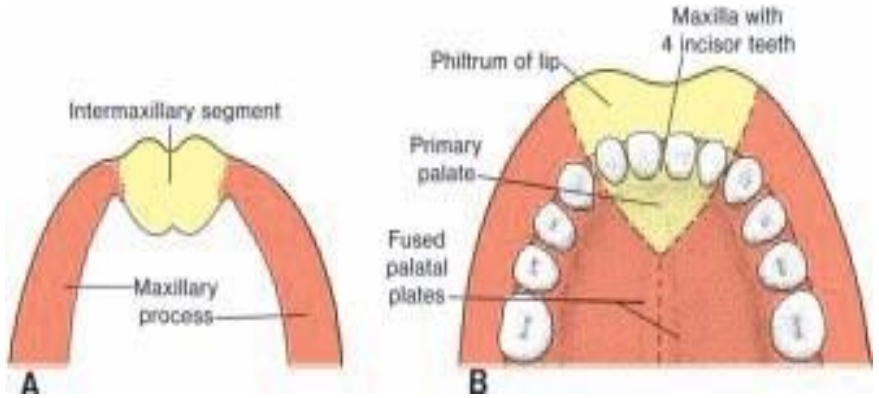
- The structure formed by the two merged prominences is the **intermaxillary segment**

- It is composed of (*a*) a **labial component,** which forms the philtrum of the upper lip;

- (*b*) an **upper jaw component,** which carries the four incisor teeth;

- (*c*) a **palatal component,** which forms the triangular primary palate

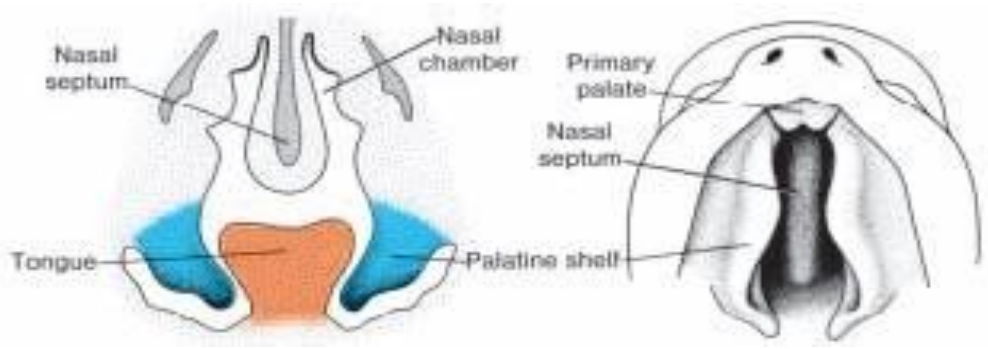
- The intermaxillary segment is continuous with the rostral portion of the **nasal septum,** which is formed by the frontal (frontonasal) prominence.



Secondary Palate

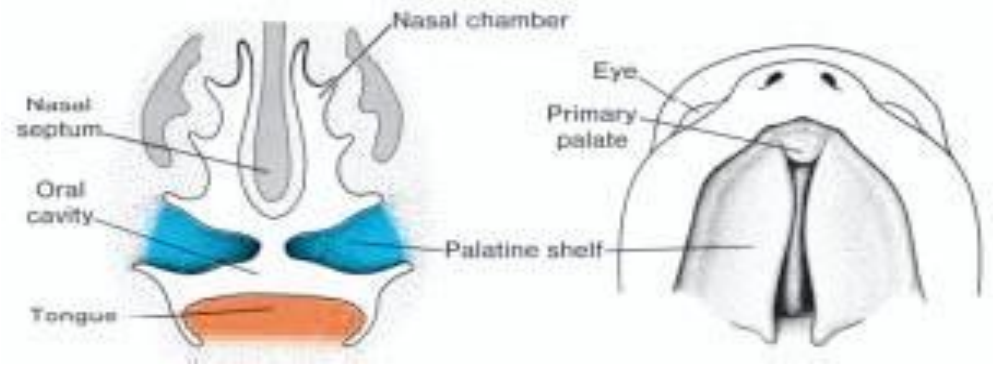
- the main part of the definitive palate is formed by two shelflike outgrowths from the maxillary prominences (maxilla)

- These outgrowths, the **palatine shelves,** appear in **the sixth week** of development and are directed obliquely downward and to the midline on each side of (above)the tongue



Secondary Palate

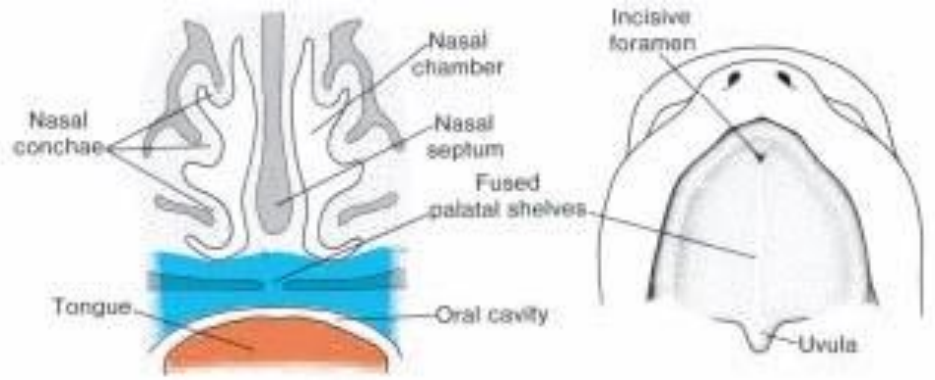
- In the **seventh week**, however, the palatine shelves ascend to attain a horizontal position above the tongue and fuse, forming the **secondary palate**



Secondary Palate

- Anteriorly, the shelves fuse with the triangular primary palate, and the **incisive foramen** is the midline landmark between the primary and secondary palates

- At the same time as the palatine shelves fuse, the nasal septum grows down and joins with the cephalic aspect of the newly formed palate



Secondary Palate

- 2 folds grow posteriorly from the edge of the palatine process to form the soft palate and the uvula.

- The union of the 2 folds of the soft palate occurs during the 8th week

- The 2 parts of the uvula fuse in the midline during the 11th week. Sometimes you notice a cleft ((شقin between which indicates the failure of complete fusion of two parts

- Unilateral cleft lip can extend to the nose (doctor said we talked about this)

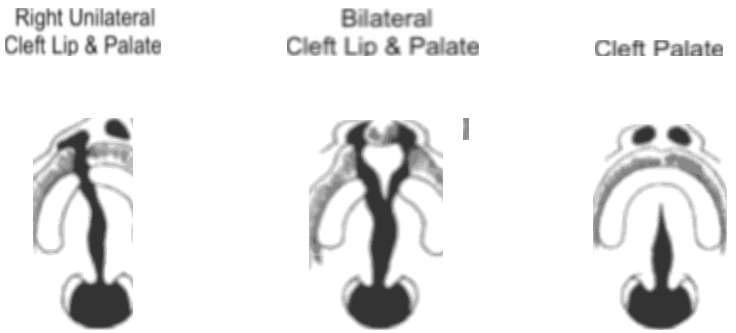
This slide is from 021 notes but I think that it is important

@ Once again and similar to cleft lip which occurs due to failure of fusion between the Maxillary Prominences and the Medial Nasal Prominences. In the case of the palate, if there is failure of fusion between the primary and secondary palates another developmental anomaly known as Cleft Palate will arise. Cleft Palate has the following characteristics:-

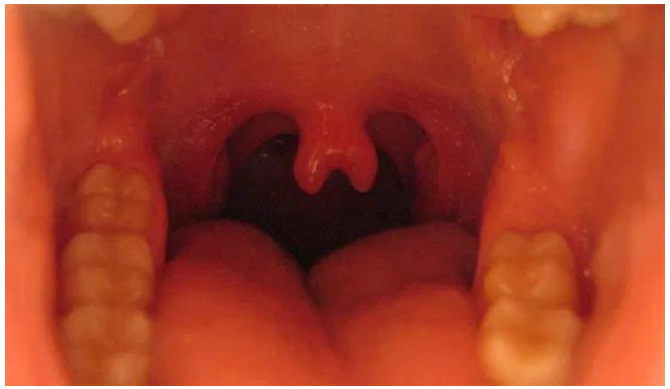
1. It could be unilateral or bilateral.

2. Unilateral cleft lip and palate can extend to the nose and nasal cavity.

3. In cleft so& palate cleft uvula can also occur

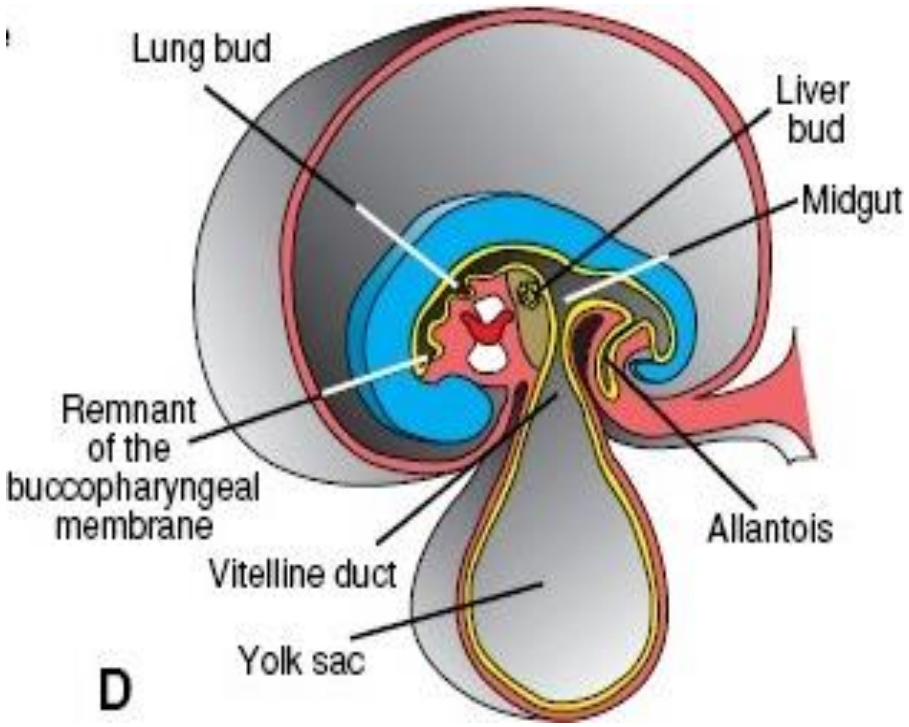


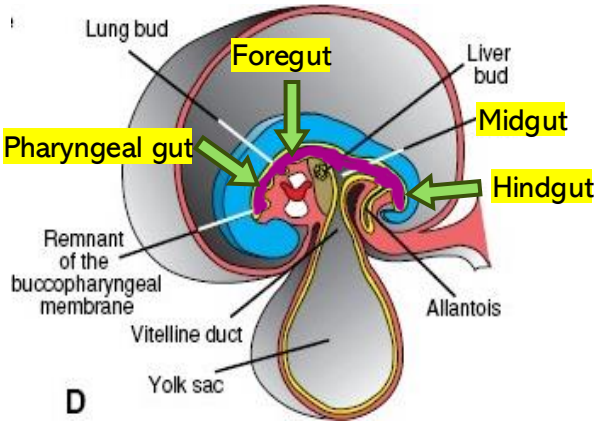
Failure of the uvulae to fuse results in a cleft uvula.



2. Development of Respiratory System

[This slide is more a revision to what is taken]
The development starts from the 4th week as we mentioned
In this picture, the blue color indicates the ectoderm
The yellow color indicate the endoderm
The red color indicate the mesoderm
This is the gut (purple below), it's divided to:
1- **anterior part (called Pharyngeal gut)** which extends from the posterior part of oral cavity to the pharynx, the pharynx is developed from the pharyngeal arches (also the pharyngeal arches are involved in the development of structures of the head and neck).
2- Foregut: from lower part of esophagus, takes stomach, until 2nd part (half) of the duodenum (liver bud).
3-Midgut: takes small intestine and large intestine until lateral 3rd (or medial 2/3rd)of transverse colon.
4-Hindgut: takes lateral 3rd of transverse colon, descending colon, sigmoid colon and anal canal.





Primitive gut

What is in green

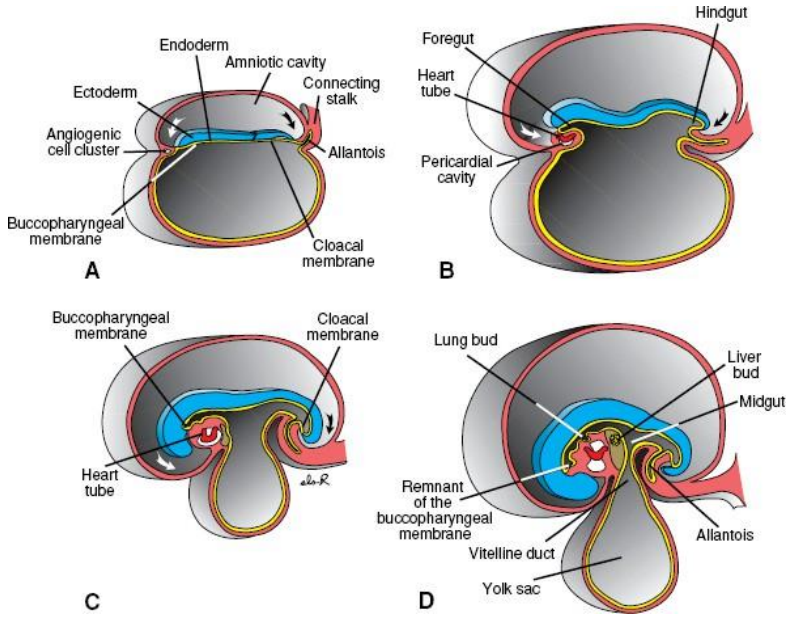
- Development of the primitive gut and its derivatives is in four sections:

- (*a*) The **pharyngeal gut,** or **pharynx,** extends from the buccopharyngeal membrane (posterior of oral cavity) to the pharynx tracheobronchial diverticulum

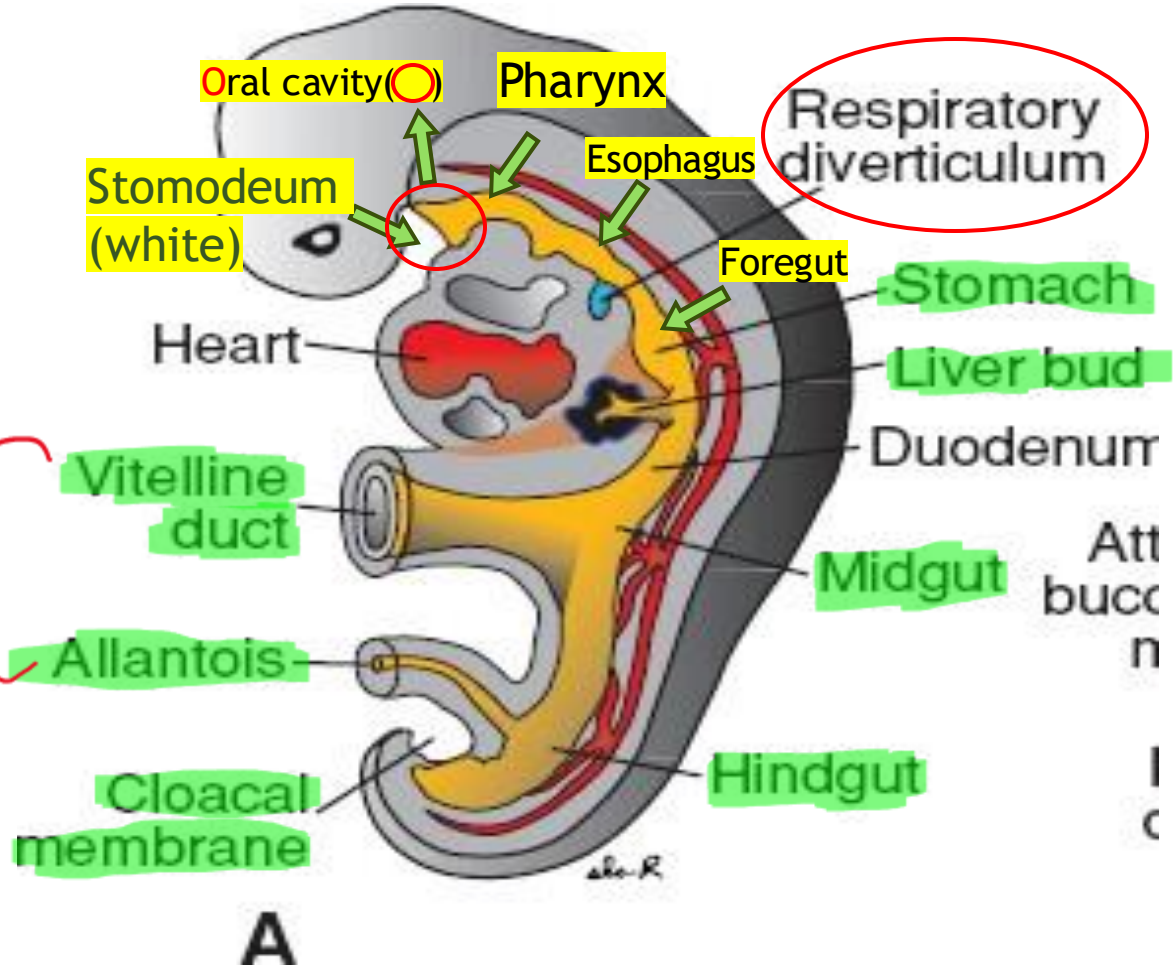
- (*b*) The **foregut** lies caudal to the pharyngeal tube (lower part of esophagus) and extends as far caudally as the liver outgrowth.

- (*c*) The **midgut** begins caudal to the liver bud and extends to the junction of the right two-thirds and left third of the transverse colon in the adult.

- (*d*) The **hindgut** extends from the left third of the transverse colon to the cloacal membrane (anal canal)



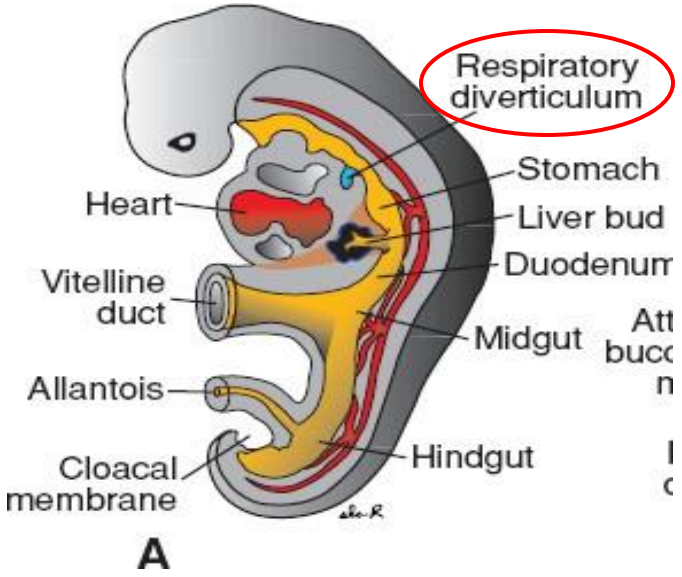
The doctor said (الي بهمني) from this draw is the respiratory diverticulum, but I'll point to the structures that he mentioned here, so it's up to you at the end =)

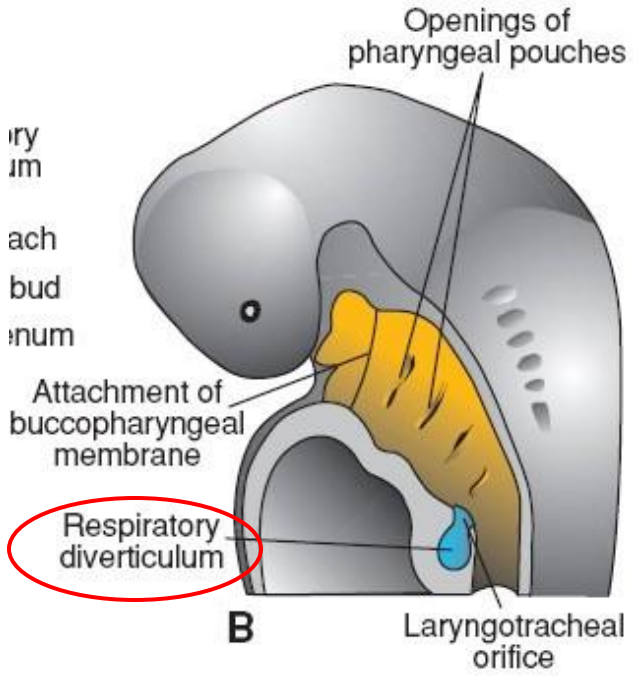


Both vitelline duct and allantois lead to umbilicus in midgut and hindgut, respectively.

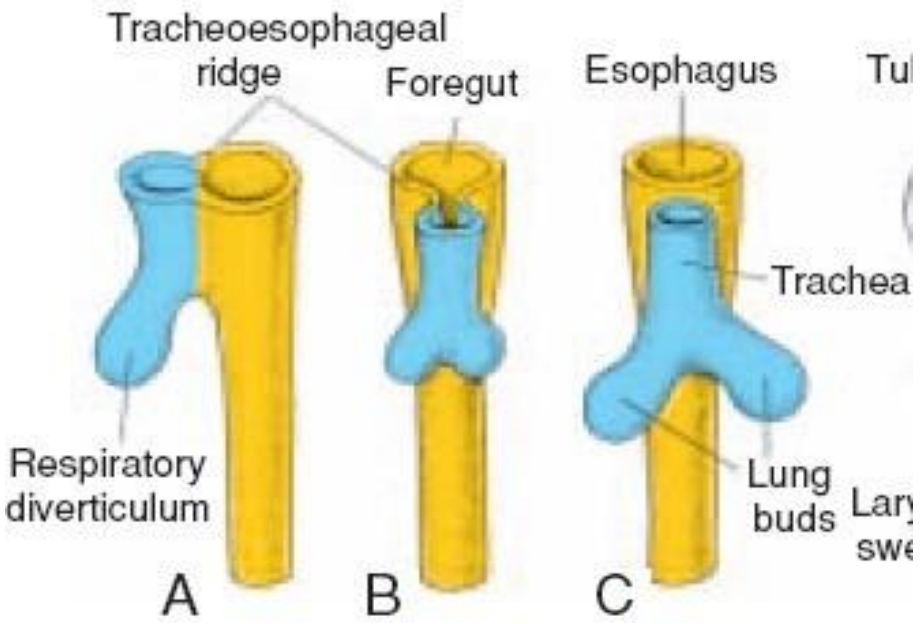
→ At the 4th week, a stimulation is received by the bud, this will stimulate the outgrowth of the cells forming the respiratory bud, the respiratory diverticulum (lung bud) outgrow from **the ventral wall of the foregut.** (This is the basis for the respiratory tract)

→ The lining epithelium of the whole respiratory diverticulum is endodermal, while the cartilage, muscle and connective tissue are derived from mesenchymal cells (mesodermal).





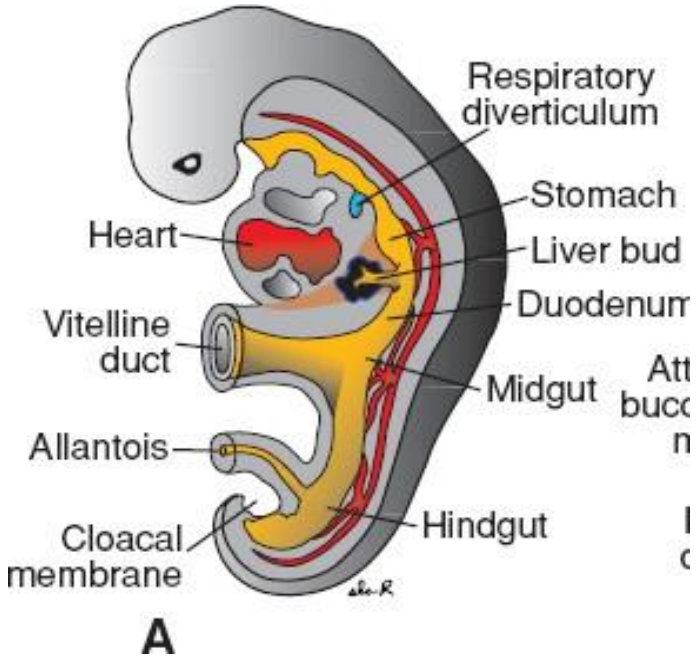
As we mentioned, there's a connection between the foregut and the respiratory diverticulum. A separation should occur between them → This occurs with the help of **tracheoesophageal ridges**, which fuse to form **tracheoesophageal septum**, it divides into dorsal portion (esophagus) and ventral portion (trachea and lung buds). The lung buds then develop to complete the respiratory tract.



Respiratory diverticulum

- When the embryo is approximately 4 weeks old, the **respiratory diverticulum** (**lung bud**) appears as an outgrowth from the ventral wall of the foregut

- The location of the bud along the guttube is determined by signals from the surrounding mesenchyme, including fibroblast growth factors (FGFs) that instruct the endoderm

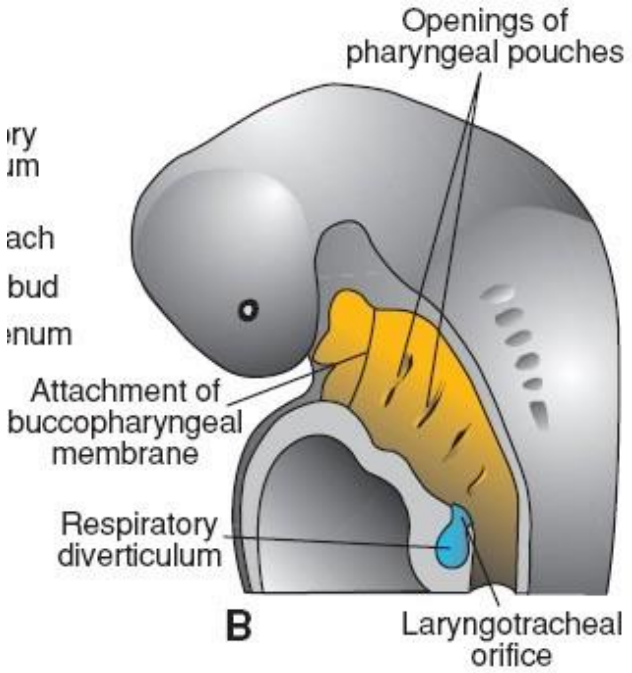


Respiratory diverticulum

- The **epithelium** of the internal lining of the larynx, trachea, and bronchi, as well as that of the lungs, is entirely of **endodermal origin.**

- The **cartilaginous, muscular,** and **connective tissue** components of the trachea and lungs are derived from **splanchnic mesoderm** surrounding the foregut.

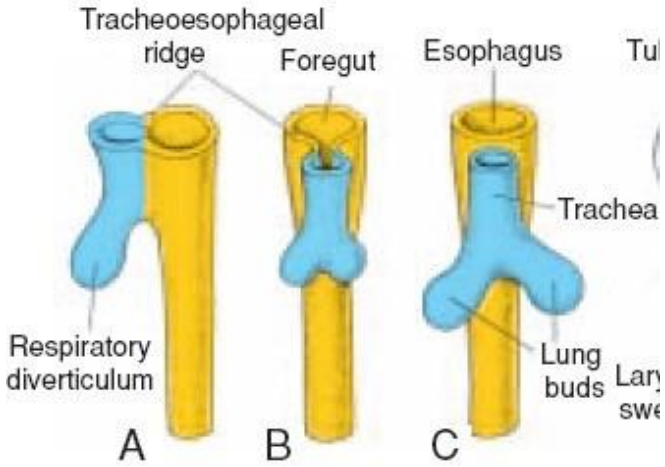
- Initially the lung bud is in open communication with the foregut



Respiratory diverticulum

- When the diverticulum expands caudally, two longitudinal ridges, the **tracheoesophageal ridges,** separate it from the foregut

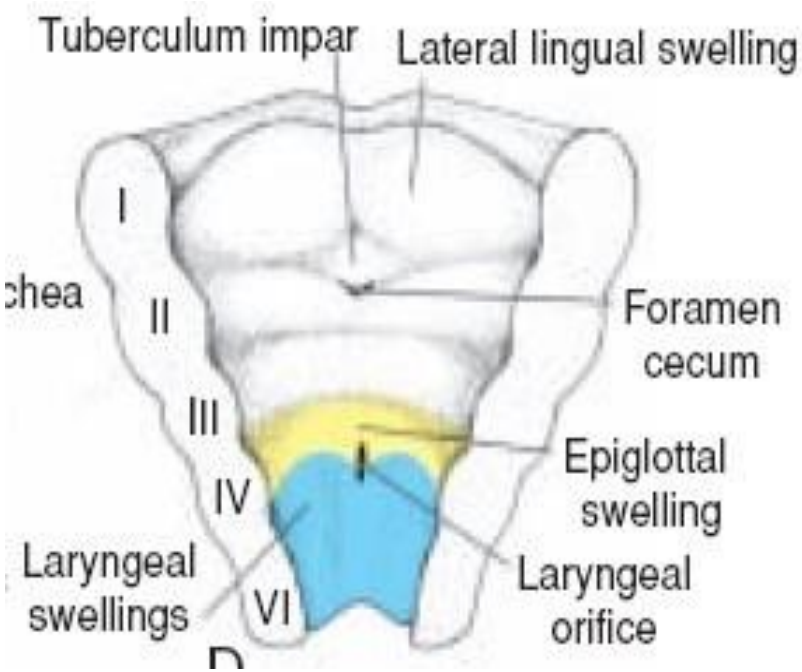
- Subsequently, when these ridges fuse to form the **tracheoesophageal septum,** the foregut is divided into a dorsal portion, the **esophagus,** and a ventral portion, the **trachea** and **lung buds**



Respiratory diverticulum

- **Q: Is there a connection between respiratory tract (larynx) and digestive tract?** Yes there is, it is the inlet of the larynx
- In the beginning, it is a laryngeal orifice that looks like vertical slit-like opening.

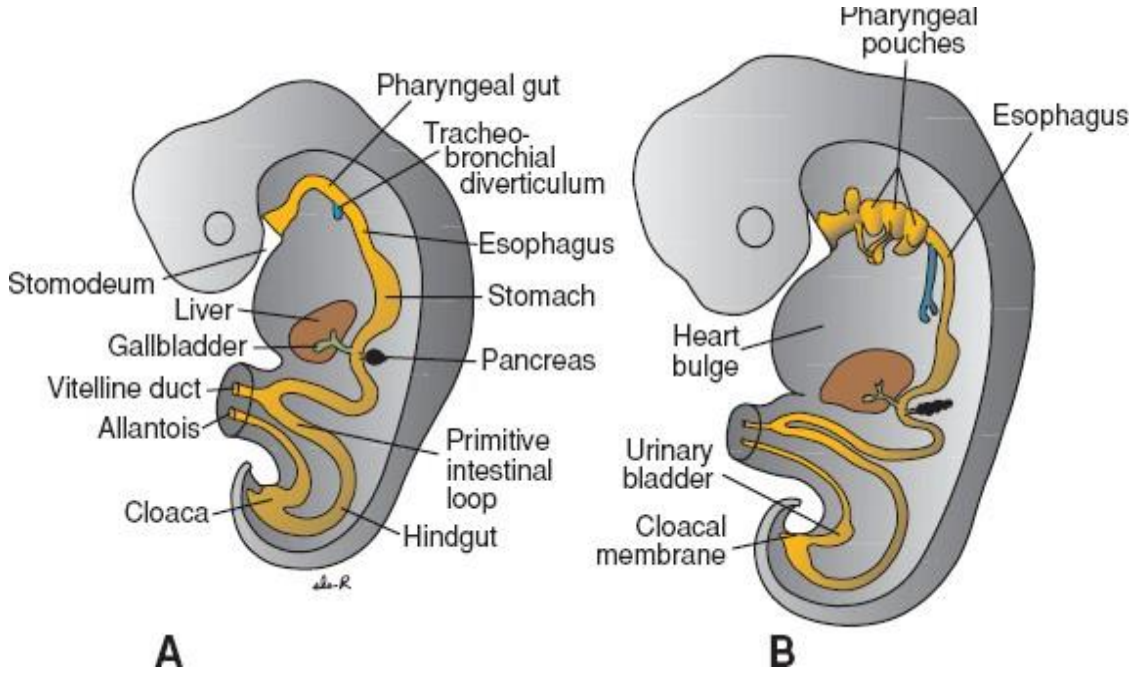
- The respiratory primordium maintains its communication with the pharynx through the **laryngeal orifice**



Esophagus

- At first the esophagus is short
- <u>but with descent of the heart and lungs it lengthens rapidly</u>
- The muscular coat, which is formed by surrounding splanchnic mesenchyme, is striated in its upper two-thirds and innervated by the vagus the muscle coat is smooth in the lower third and is innervated by the splanchnic plexus.

- As we took in GI system, the result of pericardium, heart and lung development is the descending of esophagus downward toward the abdomen.



3. Anomalies of the trachea and esophagus

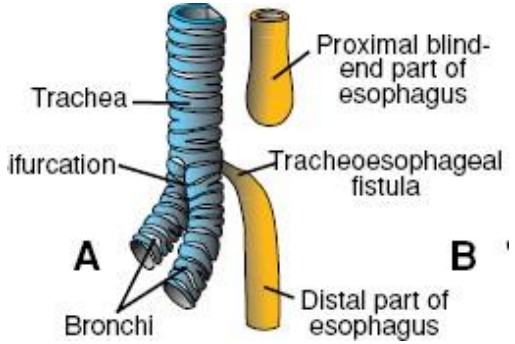
1. Tracheoesaphageal fistula (TEF)

- Abnormalities in partitioning of the esophagus and trachea by the tracheoesophageal septum result in **esophageal atresia** with or without **tracheoesophageal fistulas**

- Esophageal Atresia is the blind end of esophagus
- Tracheoesophageal fistulas is a connection between trachea and esophagus

- These defects occur in approximately in 1/3000 births, and 90% result in the upper portion of the esophagus ending in a blind pouch and the lower segment forming a fistula with the trachea **(most common case)**

- Predominantly affect male infants

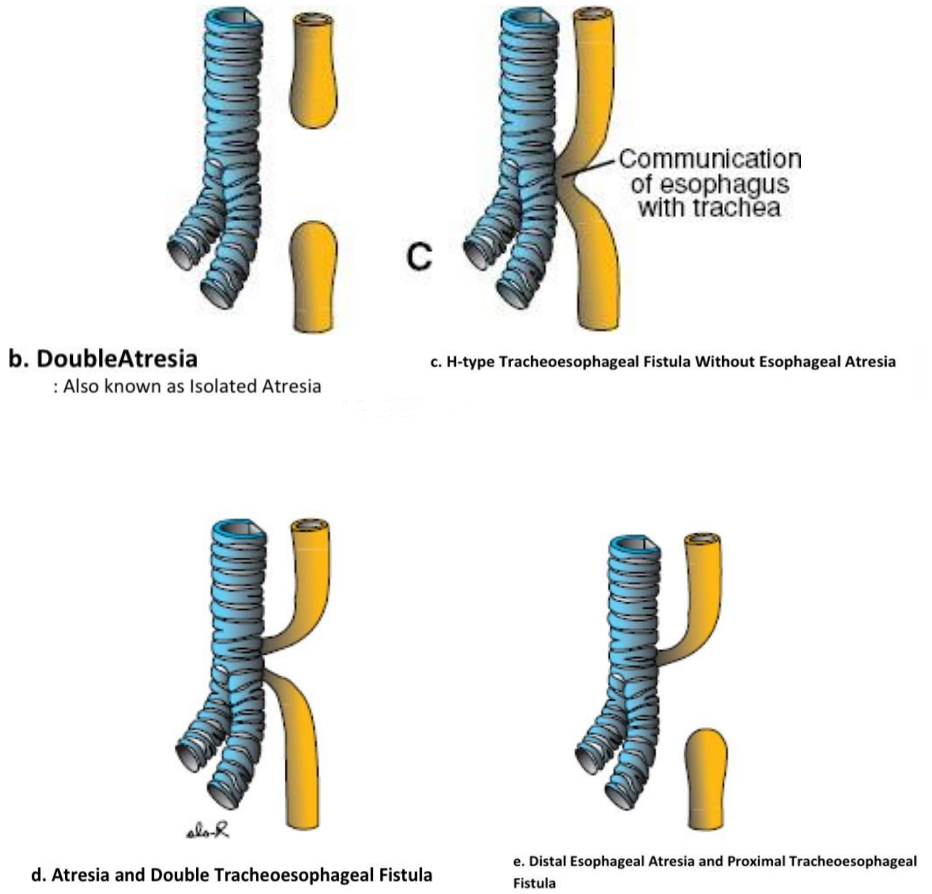


a. Proximal Esophageal Atresia with Tracheoesophageal Fistula (TEF)

(most common case)

Tracheoesaphageal fistula (TEF)

- Isolated esophageal atresia and H-type TEF without esophageal Atresia each account for 4% of these defects.
- H-type TEF mean that there is two fistula forming a shape similar to H.
- There are 4 common types of Tracheoesophageal fistulas as you see in the pic.
- Other variations each account for approximately 1% of these defects.



b. DoubleAtresia
: Also known as Isolated Atresia

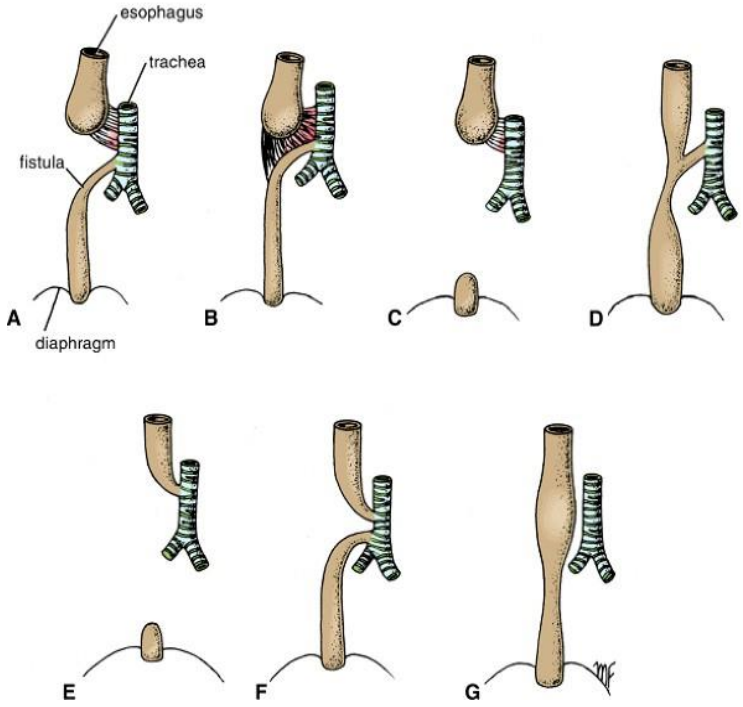
c. H-type Tracheoesophageal Fistula Without Esophageal Atresia

d. Atresia and Double Tracheoesophageal Fistula

e. Distal Esophageal Atresia and Proximal Tracheoesophageal Fistula

Tracheoesaphageal fistula (TEF)

- TEF is the most common anomaly in the lower respiratory tract
- Infants with common type TEF and esophageal atresia cough and choke because of excessive amounts of saliva in the mouth
- When the infant try to swallow milk, it rapidly fills the esophageal pouch and is regurgitated
  = ((vomiting))
- A complication of some TEFs is **polyhydramnios**, since in some types of TEF amniotic fluid does not pass to the stomach and intestines
  - **Polyhydramnios:** extra amniotic fluid before birth. [**oligohydramnios** is the opposite word], normally amniotic fluid travel to the oral cavity to GI tract and leave with urine, but fistula impedes this pathway, and return to amniotic sac, accumulation lead to polyhydramnios.
- Also, gastric contents and/or amniotic fluid may enter the trachea through a fistula, causing **pneumonitis and pneumonia**.
  - GI secretion entering the trachea can cause pneumonitis. In other cases, air may enter from the lungs into the stomach causing the infant to have a distended abdomen while crying; because the stomach is filled will air.



Tracheoesaphageal fistula (TEF)

- These abnormalities are associated with other birth defects, **including cardiac abnormalities,** which occur in **33%** of these cases. (most common)
  - The most common Cardiac abnormalities are Atrial Septal defects, Ventricular Septal defects, and Tetralogy of Fallot

- In this regard TEFs are a component of the **VACTERL** association (**V**ertebral anomalies, **A**nal atresia, **C**ardiac defects, **T**racheoesophageal fistula, **E**sophageal atresia, **R**enal anomalies, and **L**imb defects)

- a collection of defects of unknown causation, but occurring more frequently than predicted by chance alone.

2. Tracheal atresia and stenosis

- Are **uncommon** anomalies and usually associated with one of the verities of TEF

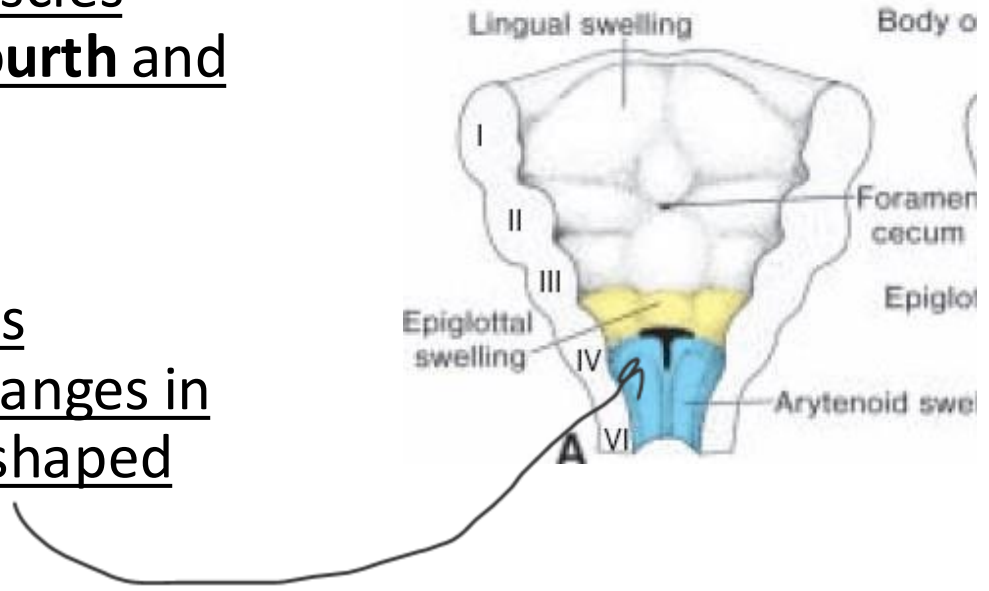
- In some case a web tissue may obstructs the airflow (incomplete tracheal atresia)

4. The development of the Larynx

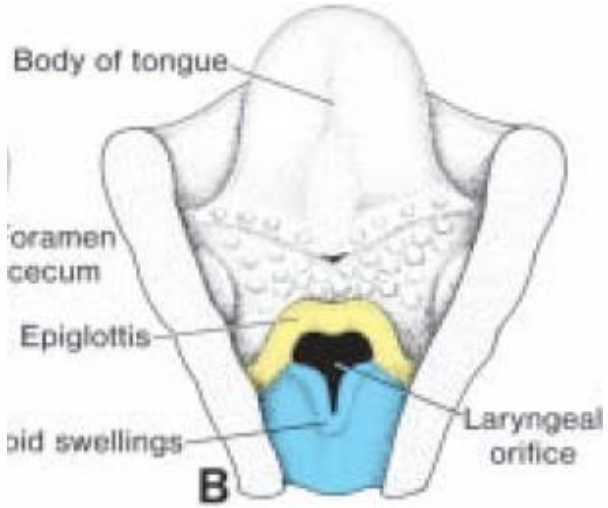
Larynx

- The internal lining of the larynx originates from **endoderm**, but the cartilages and muscles originate from **mesenchyme** of the **fourth** and **sixth pharyngeal arches**

- As a result of rapid proliferation of this mesenchyme, the laryngeal orifice changes in appearance from a sagittal slit to a T-shaped opening



- Subsequently, <u>when mesenchyme of the two arches transforms into the **thyroid, cricoid**, and **arytenoid cartilages**</u>, the characteristic adult shape of the laryngeal orifice can be recognized
- (permanent opening and consist of the epiglottis)



- At about the time that the cartilages are formed, the laryngeal epithelium(from the endoderm) also proliferates rapidly resulting in a temporary occlusion of the lumen. (filling the lumen with cells)

- Subsequently, vacuolization and recanalization produce a pair of lateral recesses, the **laryngeal ventricles** and Saccule.
- (the occlusion and the recanalization happen on the lateral side to form the ventricles and saccule, also the true and false vocal cords)

- **These recesses are bounded by folds of tissue that differentiate into the false and true vocal cords.**
  - Above the ventricle we have the false vocal cord and below it the true vocal cord.

Larynx Nerve supply

- Since musculature of the larynx is derived from mesenchyme of the fourth and sixth pharyngeal arches, all laryngeal muscles are innervated by branches of the tenth cranial nerve, the **vagus nerve** **(mainly)**

  - Vagus nerve divide into **superior** laryngeal (further divide into internal and external laryngeal), and **recurrent** laryngeal

- The **superior laryngeal** (External Laryngeal Nerve) nerve innervates derivatives of the fourth pharyngeal arch, and innervate the **cricothyroid muscle** (since its derived from the fourth pharyngeal arch)

- and the **recurrent laryngeal nerve** innervates derivatives of the sixth pharyngeal arch. (the remaining muscles is from the sixth pharyngeal arch)

- Now we can deduct the reason why all muscles of the Larynx are innervated by the Recurrent Laryngeal Nerve except the Cricothyroid which is innervated by the External Laryngeal Nerve.
- This is due to the fact that the Cricothyroid muscle is derived from the fourth pharyngeal arch and all others are derived from the Sixth.

5. Anomalies of the larynx

Laryngeal atresia

- Laryngeal atresia is a **rare** anomaly and cause obstruction of the upper fetal airway

- Also known as **congenital high airway obstruction syndrome (chaos)**

- Distal to the atresia or stenosis the lung are **enlarged** and capable of producing echoes (echogenic)
  - Obstruction leads to enlargement as you remember from patho.

- Also, the diaphragm is **flattened** or **inverted** **(goes upward)**, and fetal ascites and hydrops (accumulation of serous fluid) is present

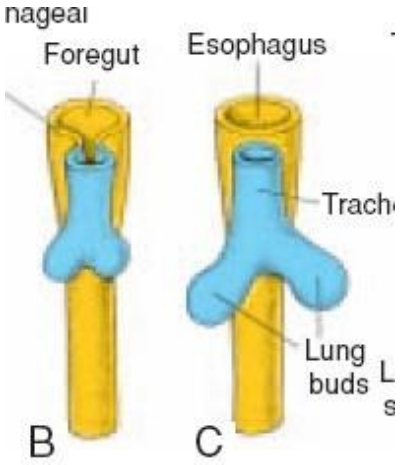
- Prenatal ultra-sonograpghy permits diagnosis.

6. The development of Lungs and Bronchial tree

Trachea, Bronchi, and Lungs

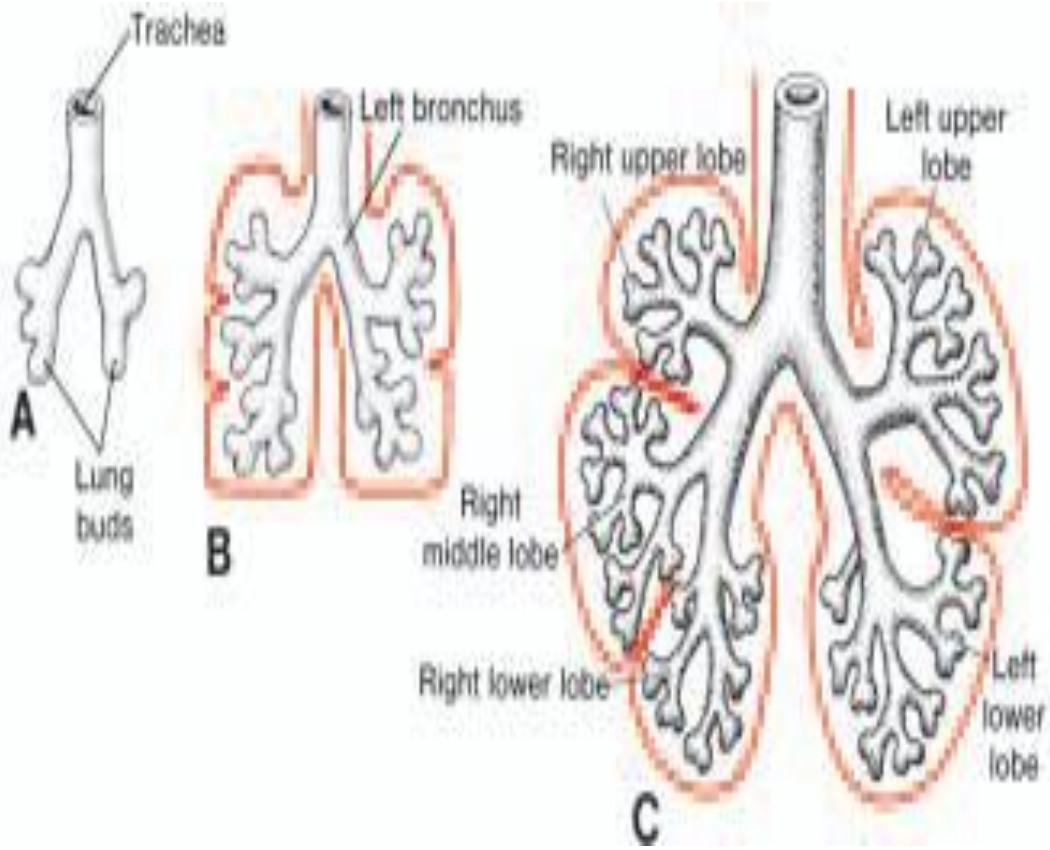
- During its separation from the foregut, the **lung bud** forms the trachea and two lateral outpocketings, the **bronchial buds**

- At the beginning of the fifth week, each of these buds enlarges to form right and left main bronchi



Trachea, Bronchi, and Lungs

- The right lung is more vertical, wider and shorter.
- The right then forms three secondary bronchi, and the left, two
- thus, foreshadowing the three lobes on the right side and two on the left
- They then continue growing into what is known as segmental or tertiary bronchi (10 on the right and 8 on the left). After birth both will be 10.



The bronchial tree

The right and left main bronchi are called the primary bronchi.

The secondary bronchi are called lobar bronchi. So, on the right side there are three lobar bronchi, since the right lung has three lobes (upper, middle and lower lobes), and on the left side there are two lobar bronchi, since the left lung has two lobes (upper and lower lobes).

-The tertiary bronchi are called bronchopulmonary segments. There are 10 bronchopulmonary segments on the right and 10 on the left in postnatal (8 on the left in embryo)

In the **right lung**:

1) The **upper** lobe has three bronchopulmonary segments: apical, anterior and posterior.
2) The **middle** lobe has two segments: medial and lateral.
3) The **lower** lobe (the base) has five segments: apicobasal (or apical), medial, lateral, anterior and posterior.

In the **left lung** in **embryo**:

1) The **upper** lobe has 4 bronchopulmonary segments: anterior, apicoposterior, superior lingual and inferior lingual.
2) The **lower** lobe (the base) has 4 bronchopulmonary segments; apicobasal (apical), posterior, anteromedial and lateral.

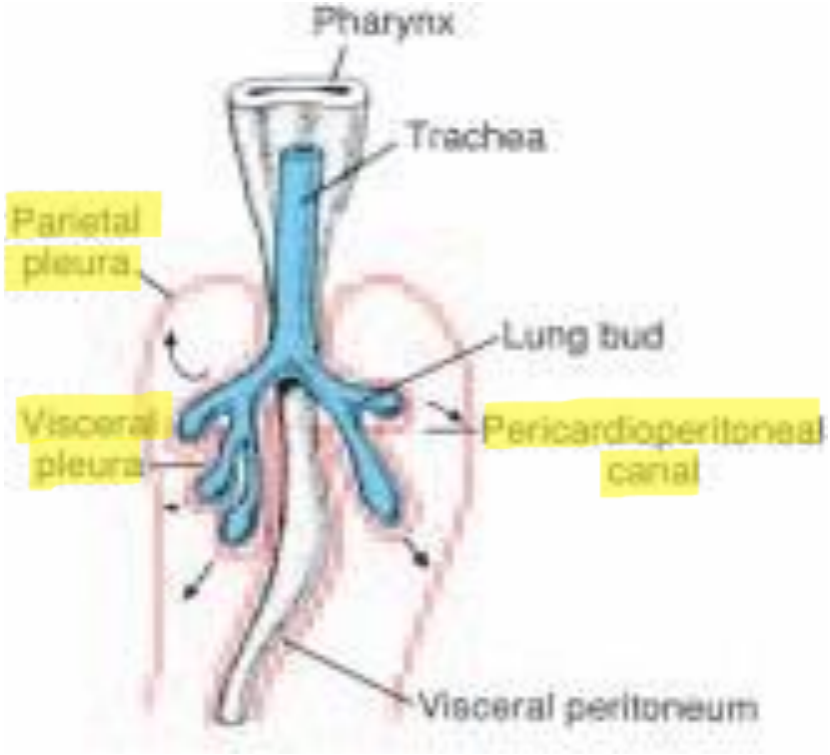
- There is a difference between the number of bronchopulmonary segments in postnatal and in an embryo. The difference is that the embryo has 8 in the left lung instead of 10. After delivery, they become 10 in number. Why is there a difference?
- In the upper lobe in the embryo, the apical and posterior segments join together as one segment called **apicoposterior**. After delivery, they are separated to give the apical and posterior segments. In the lower lobe (the base), the anterior segment and the medial segment join together forming one segment, called **anteromedial** segment. After delivery, they are also separated to give the anterior and medial segments.

Trachea, Bronchi, and Lungs

- With subsequent growth in caudal and lateral directions, the lung buds expand into the body cavity

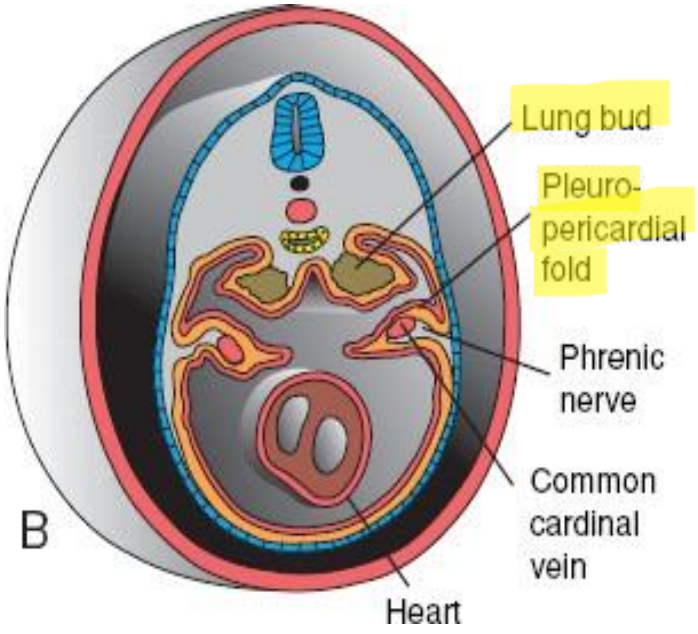
- **The spaces for the lungs, the pericardioperitoneal canals**, are narrow.
- The space where the bronchi and the lung grow and differentiate is **the pericardioperitoneal canals**

- They lie on each side of the foregut



Trachea, Bronchi, and Lungs

- Ultimately the pleuroperitoneal and pleuropericardial folds separate the pericardioperitoneal canals from the peritoneal and pericardial cavities form the **primitive pleural cavities** and remaining spaces



- Each one will separate and give :

1. **Pericardioperitoneal Cavity**

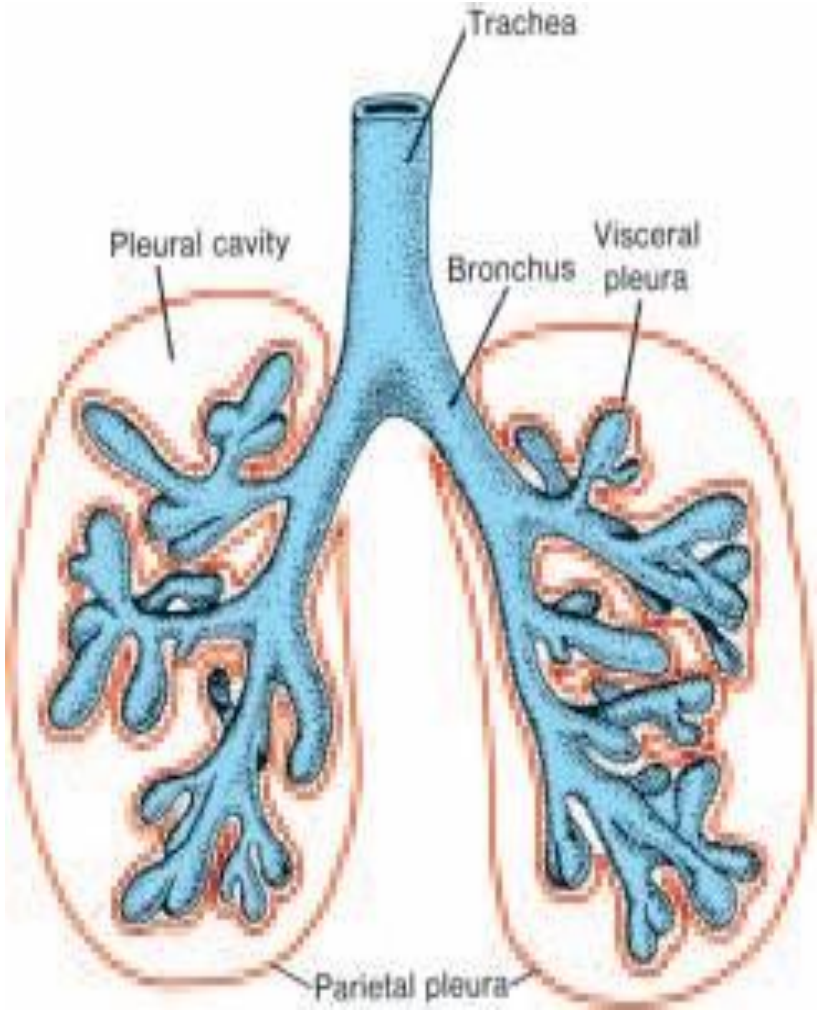
2. **Pleuropericardial Cavity** : Pleuropericardial is upward and give space to the pleura cavity, where the lung grow.

Pericardial Cavity: Surrounds the heart

Peritoneal cavity within the abdomen

Trachea, Bronchi, and Lungs

- The mesoderm, which covers the outside of the lung, develops into the **visceral pleura.**
- The somatic mesoderm layer, covering the body wall from the inside, becomes the **parietal pleura**
- The space between the parietal and visceral pleura is the **pleural cavity**



- During further development, secondary bronchi divide repeatedly in a **dichotomous** fashion, forming 10 **tertiary (segmental)** bronchi in the right lung and 8 in the left, creating the **bronchopulmonary segments** of the adult lung.

- By the end of the sixth month, approximately **17 generations** of subdivisions have formed

- Before the bronchial tree reaches its final shape, however, **an additional 6 divisions form during postnatal life.**
- Thus, as an adult we have a total of **23** generations in the respiratory tract.

- **Branching is regulated by epithelial-mesenchymal interactions between the endoderm of the lung buds and splanchnic mesoderm that surrounds them**

- Signals for branching, which emit from the mesoderm, involve members of the **fibroblast growth factor (FGF) family**.

- While all of these new subdivisions are occurring and the bronchial tree is developing, the lungs assume a more caudal position, so that by the time of birth the bifurcation of the trachea is opposite the fourth thoracic vertebra.

Maturation of the Lungs

- Doctor read all the table

There are 4 phases for the maturation if the lung

TABLE 12.1 Maturation of the Lungs

Pseudoglandular period	5–16 weeks	Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present.
Canalicular period	16–26 weeks	Each terminal bronchiole divides into 2 or more respiratory bronchioles, which in turn divide into 3–6 alveolar ducts.
Terminal sac period	26 weeks to birth	Terminal sacs (primitive alveoli) form, and capillaries establish close contact.
Alveolar period	8 months to childhood	Mature alveoli have well-developed epithelial endothelial (capillary) contacts.

Only conducting bronchioles

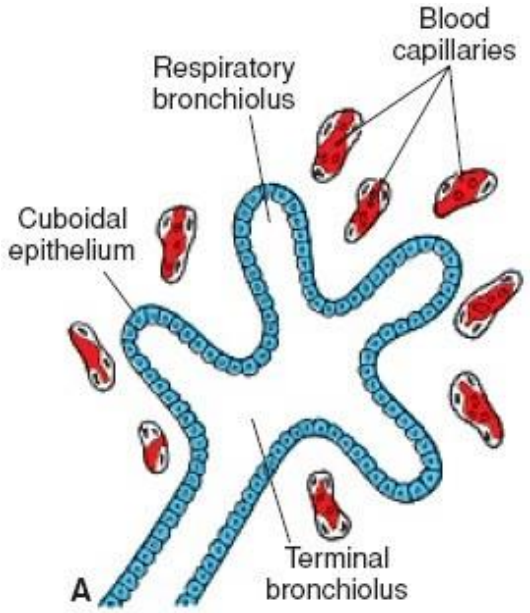
No respiratory tissue available for gas exchange before the 6th month

After the 6th month respiration can occur, so if the child is born after the 7th month the child can live

From the 8th month till 10 years-old child, the division is continuous

Maturation of the Lungs

- Up to the seventh prenatal month, the bronchioles divide continuously into more and smaller canals (canalicular phase)
- the vascular supply increases steadily.
- Respiration becomes possible when some of the cells of the cuboidal **respiratory bronchioles** change into thin, flat cells

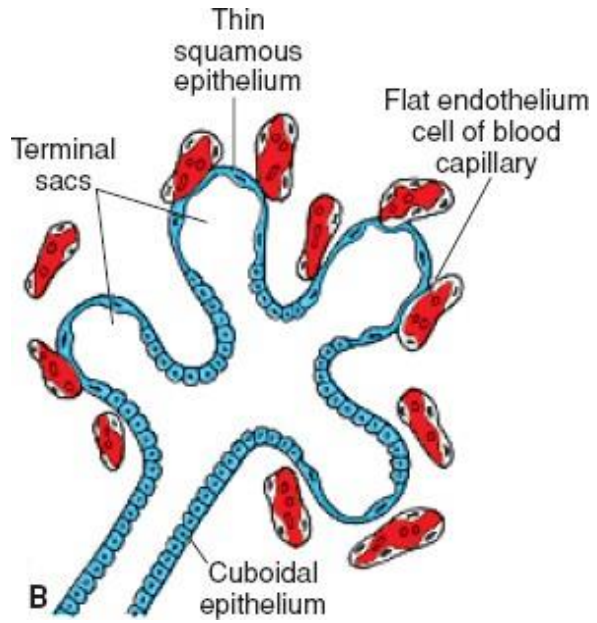


- **The canalicular phase**
- The epithelium present at this stage is simple cuboidal epithelium. (not the simple squamous epithelium typically found in respiratory part)
- The capillaries are far from each other and from the respiratory bronchioles so no formation of respiratory membrane.
- No Respiration in this Stage

Maturation of the Lungs

- These cells are intimately associated with numerous blood and lymph capillaries, and the surrounding spaces are now known as **terminal sacs** or **primitive alveoli**

- During the seventh month, sufficient numbers of capillaries are present to guarantee adequate gas exchange, and the premature infant is able to survive.



- **This brings us to an important question: Can a baby born at this stage survive?**
  - Yes, because at this stage, simple squamous epithelium would have formed and alveolar capillaries would be present, ((capillaries adhere to these flat cells forming respiratory membrane)) so gas exchange can happen.
  - Many babies are born at the 7th month of pregnancy, which almost corresponds to this stage of development, and they are able to survive.

- **The terminal sacs phase**
- The epithelium present at this stage is simple squamous epithelium that is typically found in respiratory part
- The capillaries are adherent to the respiratory bronchioles.
- Respiration occur at this Stage

Maturation of the Lungs

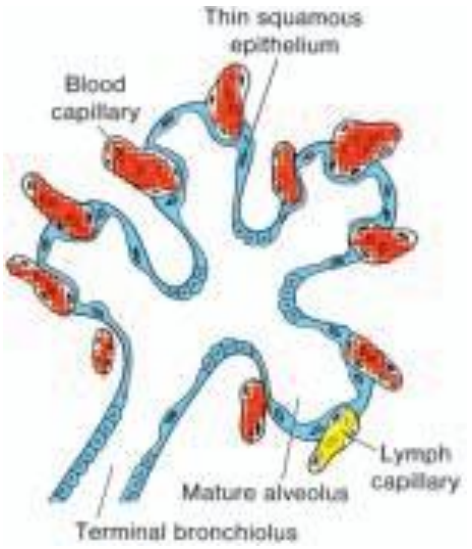
- During the last 2 months of prenatal life and for several years thereafter, the number of terminal sacs increases steadily

- In addition, cells lining the sacs, known as **type I alveolar epithelial cells,** become thinner, so that surrounding capillaries protrude into the alveolar sacs

- This intimate contact between epithelial and endothelial cells makes up the **blood-air barrier.**

- **Mature alveoli** are not present before birth

((maturation happens after birth, the alveoli before birth called primitive alveoli- still developing-.))



- **The alveolar phase**
- At this stage, all the cell is simple squamous epithelium, the alveolar capillaries have established complete contact with the alveoli.
- Type I alveolar epithelial cells, and type II alveolar epithelial cells are present.

Maturation of the Lungs

- In addition to endothelial cells and flat alveolar epithelial cells, another cell type develops at the end of the sixth month. These cells, **type II alveolar epithelial cells,** produce **surfactant,**

- Before birth the lungs are full of fluid (from cells, glands and surfactant) that contains a high chloride concentration, little protein, some mucus from the bronchial glands, and surfactant from the alveolar epithelial cells (type II)

- The amount of surfactant in the fluid increases, **particularly during the last 2 weeks before birth.**

Maturation of the Lungs

- Fetal **breathing movements** begin before birth and cause aspiration of amniotic fluid
  - Gently pat the newborn's back after birth to help clear fluids and stimulate breathing
- These movements are important for stimulating lung development and conditioning respiratory muscles

- When respiration begins at birth, most of the lung fluid is rapidly resorbed by the blood and lymph capillaries, and a small amount is probably expelled via the trachea and bronchi during delivery.

- When the fluid is resorbed from alveolar sacs, surfactant remains deposited as a thin phospholipid coat on alveolar cell membranes -type I alveolar epithelial cells-. **(surfactant membrane, very important)**

- With air entering alveoli during the first breath, the surfactant coat prevents development of an air-water (blood) interface with high surface tension

- Without the fatty surfactant layer, the alveoli would collapse during expiration **(atelectasis).**

Maturation of the Lungs

- Respiratory movements after birth bring air into the lungs, which expand and fill the pleural cavity.
- Although the alveoli increase somewhat in size, growth of the lungs after birth is due primarily to an increase in the number of respiratory bronchioles and alveoli.
- It is estimated that only one-sixth of the adult number of alveoli are present at birth
- The remaining alveoli are formed during the first 10 years of postnatal life through the continuous formation of new primitive alveoli.

7. Anomalies of the lung

1. RDS

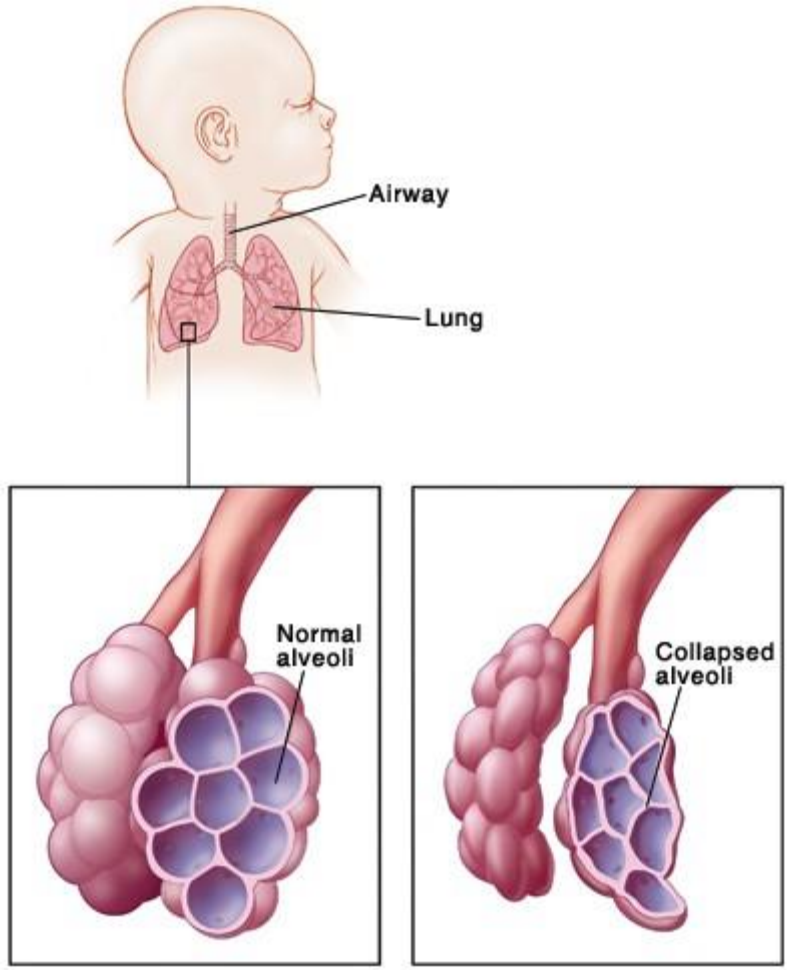
- Surfactant is particularly important for survival of the **premature infant**

- When surfactant is insufficient, the air-water (blood) surface membrane tension becomes high, bringing great risk that alveoli will collapse during expiration.

- As a result, **respiratory distress syndrome** (RDS) develops

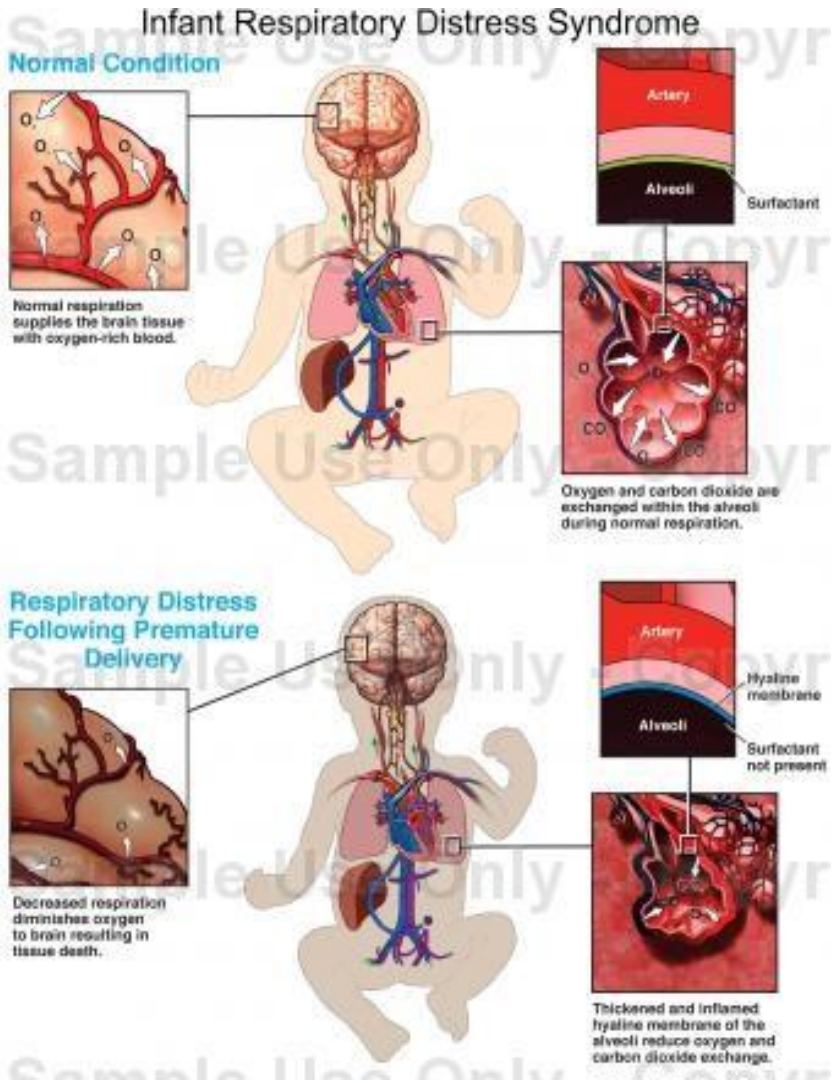
- This is a common cause of death in the premature infant (30% of all neonatal diseases)

- In these cases, the partially collapsed alveoli contain a fluid with a high protein content, many hyaline membranes, and lamellar bodies, probably derived from the surfactant layer



RDS

- RDS, is therefore also known as **hyaline membrane disease,** accounts for approximately 20% of deaths among newborns
- Intrauterine Asphyxia may produce irreversible changes in type II cells
- Recent development of artificial surfactant and treatment of premature babies with glucocorticoids (betamethasone) to stimulate surfactant production have reduced the mortality associated with RDS
- It Also allowed survival of some babies as young as 5.5 months of gestation
- **Thyroxine** is the most important stimulator for surfactants production



Clinical notes (Other Anomalies)

- Although many abnormalities of the lung and bronchial tree have been found (e.g., blind-ending trachea with absence of lungs and agenesis of one lung) most of these gross abnormalities are rare

- Abnormal divisions of the bronchial tree are more common; some result in supernumerary lobules.

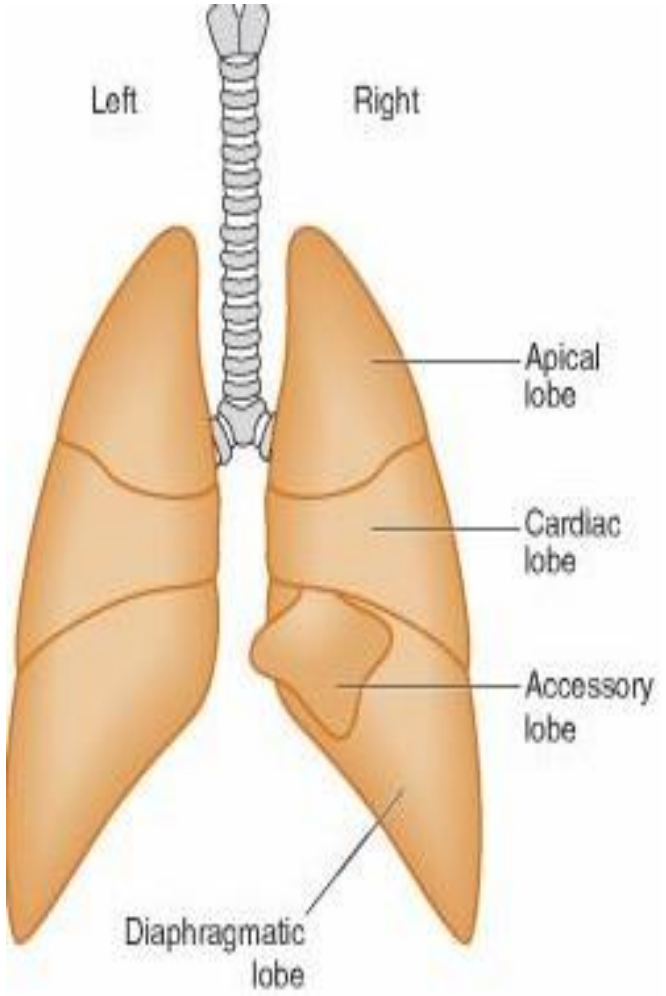
- These variations of the bronchial tree have little functional significance, but they may cause unexpected difficulties during bronchoscopies.

Clinical notes (Other Anomalies)

2. ectopic lung lobes arising from the trachea or esophagus

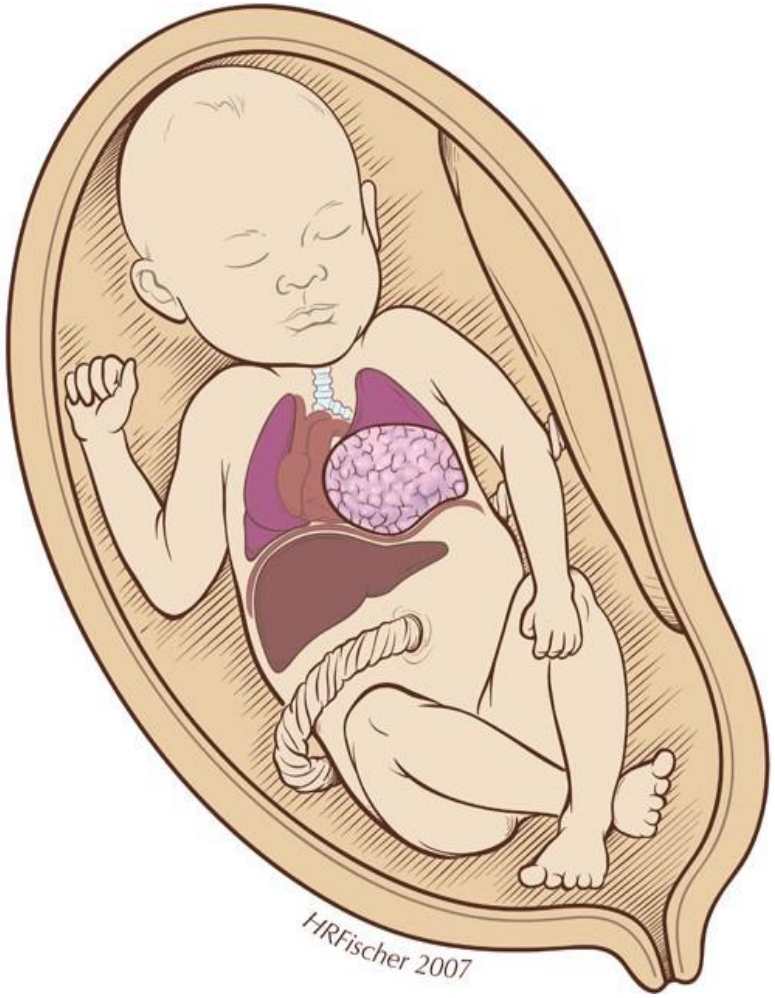
- **finding the lung in abnormal location.**
- For example, instead of 2 lobes in the left lung, there will be 4 lobes, caused by the formation of more lung buds

- It is believed that these lobes are formed from additional respiratory buds of the foregut that develop independently of the main respiratory system.



Clinical notes (Other Anomalies)

- Most important clinically are 3. **congenital cysts of the lung**
- which are formed by dilation of terminal or larger bronchi
- These cysts may be small and multiple, giving the lung a honeycomb appearance on radiograph
- May be single, or multiple
- Or they may be restricted to one or more larger ones
- Cystic structures of the lung usually drain poorly and frequently cause **chronic infections**



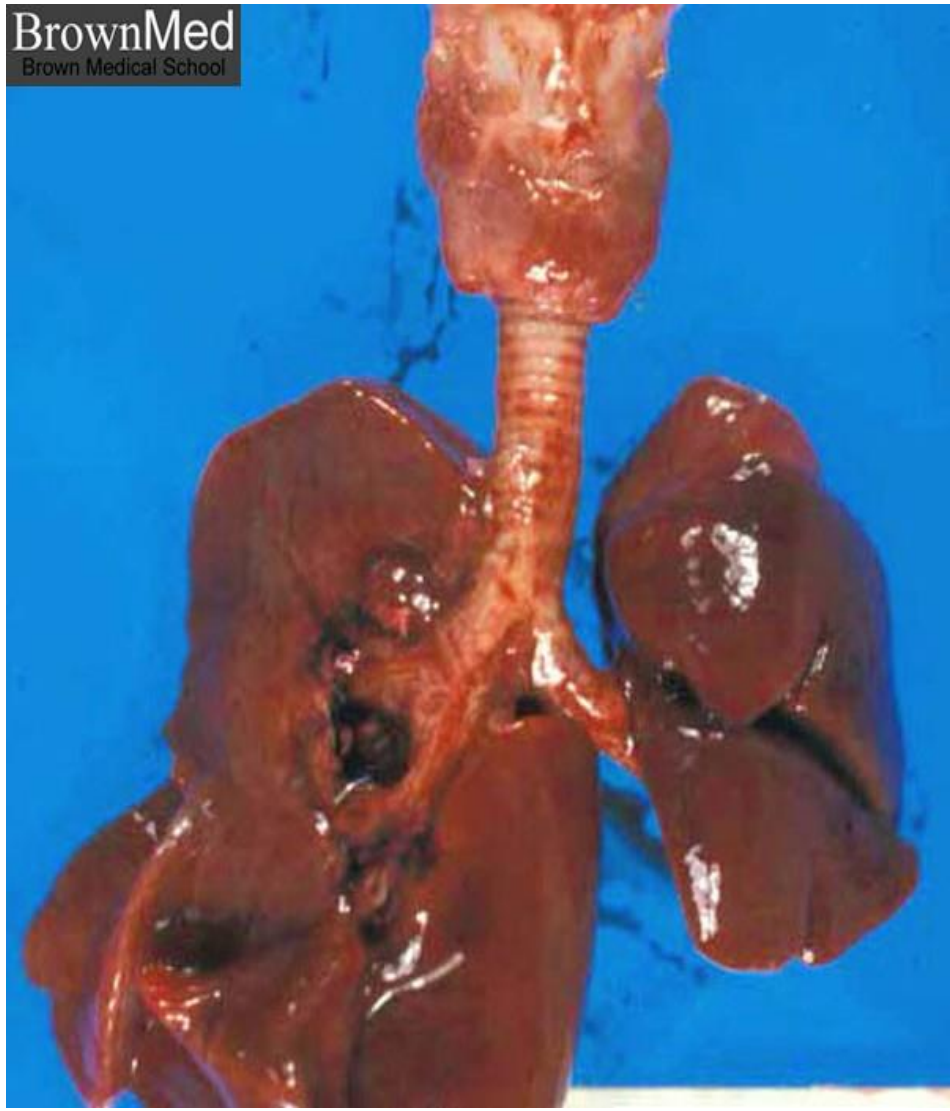
4. Lung Hypoplasia

- Shrinkage of the lung
- In infants with congenital diaphragmatic hernia (CDH) the lung is unable to develop normally (usually, the Lung Hypoplasia is with CDH)

- Because it is compressed by the abnormally positioned abdominal viscera (commonly on the left side, abdominal viscera goes upward leading to reduced volume of the left lung)

- It is characterized by reduced lung volume
- Leading to **asphyxia** (life-threatening hypoxia)

- Most infants with CDH die of pulmonary insufficiency as their lungs are too hypoplastic to support life



5. Oligohydramnios and lungs

- Amniotic fluid is important for the maturation of the respiratory tract organs

- When oligohydramnios (reduced amniotic fluid) is severe lung development is **retarded**

- Severe pulmonary hypoplasia results

Lungs of the newborn infants

- Fresh and healthy lungs contain some air so pulmonary samples float in water

- The lungs of the stillborn infants are firm and sink in water because they contain fluids not air.

*** Lastly, how can we tell if a newborn died after delivery, or if it was stillborn?** We take a sample of the lung tissue and place it in water. If it floats, it means the lungs are healthy and fresh and the baby died after delivery. If it sinks, it means no air was present in the lungs at all and the baby did not take his first breath, so it was stillborn.

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	21	Intermaxillary segment is formed by maxillary prominences	Intermaxillary segment is formed by maxillary prominences and medial nasal prominence (mostly formed by medial nasal prominence)
V2→V3 In this version, I deleted the box that says “Explained, but give it a quick read” on some slides, please make sure to read these slides, 90% of them are repetition but to be on the safe side (I distinguished these slides with empty box). I also removed number of lines under some sentences in the slides, I distinguished these sentences with dotted underline	6 / 7 / 10 / 15 / 16 / 22 / 27 / 31 33 43 62	 it's essential to note that the development of the respiratory system is largely completed by the	Highlighted Moved sentence to have clear meaning Highlighted (technical defect) This sentence had been deleted.